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A COMPARISON OF CARFENTANIL/XYLAZINE AND TELAZOL®/XYLAZINE FOR IMMOBILIZATION OF WHITE-TAILED DEER

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ABSTRACT: From October 2001 to January 2002, captive free-ranging white-tailed deer (*Odocoileus virginianus*) were immobilized with a combination of carfentanil citrate and xylazine hydrochloride. From this study, we selected a dose of carfentanil/xylazine for the purpose of comparing immobilization parameters and physiologic effects with those of a combination of tiletamine and zolazepam (Telazol®) and xylazine. Animals were initially given intramuscular injections of 10 mg xylazine and one of four doses of carfentanil (i.e., 0.5, 1.0, 1.5, and 2.0 mg). A carfentanil dose of 1.2 mg ($\bar{x}\pm$SD=23.5±3.2 μg/kg) and 10 mg xylazine (0.2±0.03 mg/kg) were selected, based on induction times and previously published reports, to compare with a combination of 230 mg of Telazol® (4.5±0.6 mg/kg) and 120 mg xylazine (2.3±0.3 mg/kg). Time to first observable drug effects and to induction were significantly longer for deer treated with carfentanil/xylazine than with Telazol®/xylazine ($P<0.01$). Hyperthermia was common in deer immobilized with carfentanil/xylazine, but heart rate, respiration rate, and hemoglobin saturation were within acceptable levels. Degree of anesthesia of deer immobilized with Telazol®/xylazine was superior to deer immobilized with carfentanil/xylazine. The combination of 120 mg of naltrexone hydrochloride and 6.5 mg of yohimbine hydrochloride provided rapid and complete reversal (1.9±1.1 min) of carfentanil/xylazine immobilization. Animals immobilized with Telazol®/xylazine had long recovery times with occasional resedation after antagonism with 6.5 mg of yohimbine. The combination of carfentanil and xylazine at the doses tested did not provide reliable induction or immobilization of white-tailed deer even though drug reversal was rapid and safe using naltrexone and yohimbine.

Key words: Carfentanil citrate, hyperthermia, induction, naltrexone hydrochloride, *Odocoileus virginianus,* reversal, Telazol®, white-tailed deer, yohimbine hydrochloride.

INTRODUCTION

Remote chemical immobilization is often necessary for research and management of white-tailed deer (*Odocoileus virginianus*). Although improvements in immobilizing drug combinations and remote delivery equipment have increased animal recovery rates, more improvements are needed (Kilpatrick et al., 1996). The ideal capture drug should be safe, have a short induction time, a wide safety margin, produce no long-term effects, require only a small volume (facilitating remote delivery), and be completely reversible. Currently, no drug or combination of drugs meets these criteria.

The most commonly recommended drug combination for remote immobilization of free-ranging white-tailed deer is tiletamine and zolazepam (Telazol®) and xylazine hydrochloride (Kreeger, 1996; Kilpatrick and Spohr, 1999). Deer have also been successfully immobilized with a combination of ketamine hydrochloride and xylazine. However, Kilpatrick and Spohr (1999) documented shorter flight distances and smaller search areas for deer darted with Telazol®/xylazine compared to ketamine/xylazine.

The combination of Telazol®/xylazine (T/X) has been very effective and safe in field conditions (Kilpatrick and Spohr, 1999; Murray et al., 2000). However, this combination may require an extended recovery time for animals (Millspaugh et al.,

1995; Nielsen, 1999). A long recovery may lead to increased mortality from predation, adverse environmental conditions, or intraspecific fighting.

Carfentanil citrate, an ultra-potent opioid, when combined with xylazine has been effective for chemical immobilization of large cervids. This combination of carfentanil/xylazine (C/X) has demonstrated short induction times, wide safety margins, and low volumes in certain species (Kock and Berger, 1987; Haigh, 1991; Miller et al., 1996). Furthermore, it is rapidly and completely reversible with a combination of naltrexone hydrochloride and yohimbine hydrochloride (Meuleman et al., 1984; Haigh, 1991; Miller et al., 1996). However, excitability prior to induction, loss of thermoregulatory capabilities, respiratory depression, muscle rigidity, bradycardia in high doses, vomition, defecation, temporary endocrine changes, and potential for narcotic recycling are major side effects observed in some species (Haigh, 1990; Kreeger, 1996; Nielsen, 1999). There has been no substantial testing of its effectiveness for chemical immobilization of white-tailed deer. This study compared immobilization parameters and physiologic effects of C/X with those of T/X in white-tailed deer.

MATERIALS AND METHODS

All research was conducted at the University of Georgia Daniel B. Warnell School of Forest Resources Whitehall Deer Research Facility (33°53′N, 83°21′W). Research protocols received prior approval from the University of Tennessee and the University of Georgia Animal Care and Use Committees (UT-ACUC# 1141, UGA ACUC# A2002-10062-0). The weight of tested animals was 52.1±8.7 kg. Deer were housed in large (0.4–0.8 ha) outdoor pens with food and water available ad libitum. Deer were moved to 3×6 m stalls 24–36 hr prior to treatments. Food was withheld from deer beginning 12–16 hr before immobilization.

Deer were assigned randomly to treatments administered in a squeeze chute via intramuscular (IM) injection in the hindquarter for Studies 1, 2, and 3. Immediately after drug injection, they were released into a 15×20 m observation pen where observers recorded time for first noticeable drug effect (e.g., stumbling, change in movement pattern and behavior) and induction time (when deer collapsed and remained immobile). When each deer became recumbent, the deer was moved, treated with ophthalmic ointment (Paralube® Vet Ointment, Pharmaderm, Melville, New York, USA) to prevent corneal drying, masked, and weighed to the nearest 0.45 kg. Heart rate (determined by auscultation), respiration rate (observed by thoracic movements), rectal temperature (B-D Digital Fever Thermometer, Becton Dickinson, Franklin Lakes, New Jersey, USA), and hemoglobin saturation (pulse oximeter with probe on the tongue, Ohmeda Biox 3700, Ohmeda, Louisville, Colorado, USA) were recorded at 5–10 and 15–20 min after induction (Studies 1, 2, and 3). The maximum temperature measurable by the thermometer was 42.2 C. Therefore temperatures ≥42.2 C were recorded as 42.2 C.

Approximately 30 min after induction, each deer was taken to an individual stall for antagonist administration (Studies 1 and 3). All deer were periodically checked for signs of resedation for 24 hr following antagonist administration. To avoid arousing any resedated deer, all night checks were made in complete darkness with the use of night vision equipment (ITT Night Quest Model 160, ITT, Roanoke, Virginia, USA). Time periods from injection of agonists to induction (C/X and T/X treated deer; Studies 1, 2, and 3) and time periods from injection of antagonist until standing (C/X-treated deer; Studies 1 and 3) were videotaped for further evaluation.

Regression analysis for general linear models was used to evaluate the relationship among induction times, physiologic measurements, and carfentanil dose. Relationships between ambient temperatures and rectal temperatures were examined by correlation. Differences between groups were analyzed using paired *t*-tests and the Wilcoxon Signed Rank test for non-normal data (SAS Institute, Cary, North Carolina, USA). We used a 2-way analysis of variance to compare effects of drug, sex, and possible interactions for Study 3 (SAS Institute). If no significant differences in physiologic values were detected between time periods, values were combined and used to test for differences between drug treatments.

Study 1: Selection of carfentanil dose

Study 1 examined effectiveness of carfentanil doses 0.5, 1.0, 1.5, and 2.0 mg. Nineteen captive white-tailed deer (10 males, nine females; ≥1.5 yr old) were immobilized with carfentanil (3 mg/ml; Wildnil®, Wildlife Laboratories, Inc., Fort Collins, Colorado, USA) and xylazine (100

mg/ml Cervizine®, Wildlife Laboratories, Inc.) between 8 and 31 October 2001. Ten of these deer were immobilized on two separate occasions with a 3 wk period between treatments. Deer were randomly assigned to one of four treatment groups (i.e., 0.5, 1.0, 1.5, or 2.0 mg carfentanil). Four males and four females were given a carfentanil dose of 0.5, 1.0, and 1.5 mg. One doe was excluded from the analysis for the 1.0 mg group because she did not receive a complete injection. Three males and three females were given a carfentanil dose of 2.0 mg. Each dose of carfentanil was combined with 10 mg xylazine. We chose fixed doses of carfentanil and xylazine to reflect the situation most useful in the field where body weights cannot be obtained before treatment. Upon obtaining body weights, actual carfentanil doses ranged from 7.8–46.8 μg/kg and xylazine doses ranged from 0.16–0.27 mg/kg. Immobilization was reversed with naltrexone (50 mg/ml, Trexonil®, Wildlife Laboratories, Inc.) administered at 100 times the carfentanil dose (Allen, 1996) and 5 mg yohimbine (5 mg/ml, Antagonil®, Wildlife Laboratories, Inc.). Yohimbine doses ranged from 0.08–0.14 mg/kg body weight. After yohimbine was given intravenously (IV), naltrexone was given half IV and half subcutaneously (SC). Time from injection of naltrexone until the deer was standing was recorded to the nearest second.

Study 2: Recovery of carfentanil-treated deer without the use of antagonists

Study 2 was designed to evaluate the safety of carfentanil without the use of antagonists. Two male and two female deer, ≥1.5 yr old, were immobilized on 22 January 2002 with 1.2 mg carfentanil and 10 mg xylazine. After induction, physiologic measurements were recorded at 5–10 and 15–20 min as before, and then heart rate, respiration rate, and rectal temperature were taken approximately every 30 min until the animals were unapproachable. Duration of immobilization was recorded as the time from induction until the deer was standing. Ambient temperatures during immobilization were recorded.

Study 3: Comparison of carfentanil/xylazine to Telazol®/xylazine for immobilization of white-tailed deer

On 20 December 2001, 16 deer (eight males, eight females; ≥1.5 yr old) were assigned randomly to the C/X or T/X treatment groups. Eight deer were immobilized with a combination of 1.2 mg of carfentanil (doses=17.8–29.0 μg/kg) and 10.0 mg of xylazine (doses=0.15–0.24 mg/kg), and eight deer were immobilized with a combination of 230 mg Telazol® (doses=3.4–5.7 mg/kg) (100 mg/ml, Fort Dodge Animal Health, Fort Dodge, Iowa, USA) and 120 mg of xylazine (doses=1.7–3.0 mg/kg). After induction, physiologic measurements were recorded as before. The drug treatment groups were switched in each deer 2.5 wk later. Ambient temperature at time of agonist injection was recorded.

Immobilization was reversed using naltrexone (100 times the carfentanil dose) combined with 6.5 mg yohimbine in a single syringe for C/X treated deer and 6.5 mg yohimbine for T/X treated deer. All reversal drugs were given half IV and half SC. Any T/X treated deer that showed no signs of reversal after 120 min were given an additional 10 mg yohimbine (half IV and half IM). Time of reversal was recorded to the nearest second for C/X treated deer and to the nearest minute for T/X treated deer.

RESULTS

Study 1: Selection of carfentanil dose to immobilize white-tailed deer

A combination of 0.5–2.0 mg carfentanil and 10 mg xylazine was evaluated with 29 immobilizations of 19 deer. Time to first noticeable drug effects occurred from 0.7–3.5 min and included stumbling and changes in gait patterns. Excitability was observed in most animals. Deer ran around the observation pen in circles, often unconcerned or unaware of the presence of nearby human observers. Rear limb ataxia was common prior to induction. Two deer flipped onto their backs from loss of hind-leg control; however, they suffered no ill effects. Generalized muscle fasciculations, lasting 5–10 min post-induction, were common in sternally or laterally recumbent animals. Urination and penile erections were observed in males on two occasions.

Induction times ranged from 2.2–8.7 min. Linear regression of carfentanil dose verses induction time was significant. However, due to variability of induction times, the linear model was a poor predictor of the relationship (r^2=0.17; Fig. 1). Quality of immobilization was inconsistent at a particular dose. Some deer were immobilized completely, whereas others were responsive to noise or touch. The

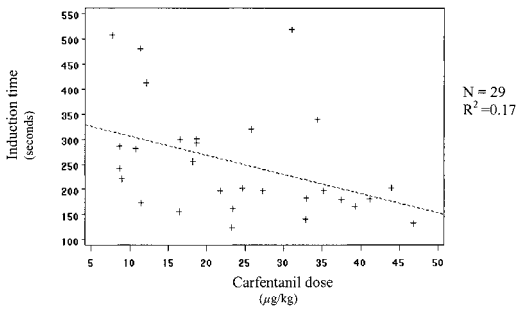

FIGURE 1. Induction times for captive white-tailed deer immobilized intramuscular with 0.5–2.0 mg carfentanil (7.75–46.84 μg/kg) and 10 mg xylazine (0.16–0.27 mg/kg).

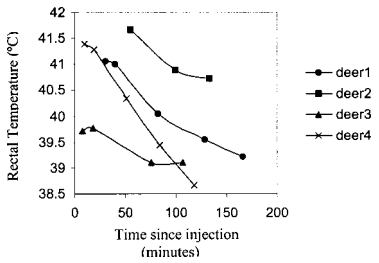

FIGURE 2. Rectal temperatures of captive white-tailed deer immobilized with 1.2 mg carfentanil and 10 mg xylazine. Maximum temperature measurable by the thermometer was 42.2 C and no observations were recorded until temperatures fell to measurable levels.

variability did not appear to relate to the carfentanil dose even when accounting for the amount of drug given per body weight.

A dose of 1.2 mg carfentanil ($\bar{x}$=23.5±3.2 μg/kg) combined with 10 mg of xylazine ($\bar{x}$=0.2±0.03 mg/kg) was chosen for all further testing. Lower carfentanil doses resulted in long induction times, and higher doses did not show dramatic improvement in induction times (Fig. 1). All reversals were rapid after injection of antagonist. Reversal times were $\bar{x}$=2.6±1.7 min. Only one deer showed signs of narcotic recycling. A female that received a carfentanil dose of 34.4 μg/kg appeared drowsy and reluctant to rise 1.5 hr after reversal. All other deer appeared alert and fully coordinated after drug reversal.

One deer sustained a lower lip avulsion after colliding with a fence, and required sutures. Hyperthermia (rectal temperatures ≥41.1 C) was observed in 13 of 29 immobilizations. All other physiologic parameters were within acceptable ranges. No health complications resulting from immobilization and reversal of C/X were observed in the deer within 3 mo after treatment.

Study 2: Recovery of carfentanil-treated deer without the use of antagonists

Mean duration of immobilization for C/X-treated deer was 3.5±0.8 hr. Three to five physiologic measurements were taken during immobilization per deer. There was no significant relationship between heart rate (24–66 beats/min), or respiration rate (7–30 breaths/min) and duration of immobilization (P>0.05). Rectal temperatures were negatively related with duration of immobilization (P<0.05) (Fig. 2). Ambient temperatures ranged between 10 and 15 C during trials. One deer fractured its mandible during induction and was euthanized after recovery from immobilization. Other deer recovered without incident.

Study 3: Comparison of carfentanil/xylazine to Telazol®/xylazine for immobilization of white-tailed deer

All deer injected with C/X or T/X were successfully immobilized. All deer were hand-injected in the squeeze chute except one; this deer was physically restrained by two people for injection. Times until first noticeable drug effect and induction were shorter (P<0.01) with T/X treated deer than C/X treated deer (Table 1). Times until induction were longer in males than females for both drug treatments (CX male=6.1±3.8 min, CX female=3.2±2.1 min, TX male=2.6±0.9 min, TX female=2.2±0.5 min).

Degree of immobilization was inconsistent among the 16 C/X treated deer. One male had to be reversed before all physiologic measurements could be taken due to an insufficient degree of anesthesia. Four other C/X treated deer were respon-

TABLE 1. Chemical immobilization of 16 captive white-tailed deer (eight male and eight female adults; Study 3) using 1.2 mg carfentanil and 10 mg xylazine (C/X) or 230 mg Telazol® and 120 mg of xylazine (T/X) and reversal by 120 mg of naltrexone and 6.5 mg of yohimbine (N/Y) or 6.5 mg yohimbine (Y).

	Agonist		Antagonist	
	C/X mean±SD (*n*) (range)	T/X mean±SD (*n*) (range)	N/Y mean±SD (*n*) (range)	Y mean±SD (*n*) (range)
Time to first effect (min)	1.8 ± 0.6 (16) (0.4–3.0)	1.4 ± 0.3 (16) (0.9–2.1)		
Induction time (min)	4.7 ± 3.3 (16) (0.5–11.7)	2.4 ± 0.7 (16) (1.1–4.6)		
Reversal time (min)			1.9 ± 1.1 (16) (0.6–5.0)	165.5 ± 66.4 (13)[a] (69–259)

[a] Ten animals still immobilized after 120 min were given an additional 10 mg yohimbine.

sive to sound or touch; however, all measurements were obtained. All T/X treated deer demonstrated excellent immobilization.

There were no differences between sexes for any of the physiologic measurements. Respiration rates, heart rates, and rectal temperatures (Table 2) did not differ between the two time periods measured for C/X treated deer or T/X treated deer. Respiration rates and heart rates did not differ ($P>0.05$) between C/X and T/X treated deer.

Rectal temperatures were higher ($P<0.01$) in C/X treated deer than in T/X treated deer. Nine of 16 deer immobilized with C/X had rectal temperatures ≥41.1 C; however, only two of 16 deer immobilized with T/X had rectal temperatures ≥41.1 C. No correlation was found between ambient temperature at time of agonist injection and rectal temperature 15–20 min post-induction for C/X treated deer ($r=0.08$, $P>0.05$) or T/X treated deer ($r=-0.28$, $P>0.05$).

Hemoglobin saturations did not differ between the two time periods for C/X treated deer ($P>0.05$); however, hemoglobin saturations for T/X treated deer were greater ($P<0.05$) in the second time period. Hemoglobin saturations were not different ($P=0.07$) in the first time period between C/X treated deer and T/X treated deer. Hemoglobin saturations were higher

TABLE 2. Physiologic data from 16 captive white-tailed deer (eight male and eight female adults; Study 3) immobilized with 1.2 mg of carfentanil and 10 mg xylazine (C/X) or 230 mg Telazol® and 120 mg xylazine (T/X).

Time post-induction (min)	C/X mean±SD (*n*) (range)		T/X mean±SD (*n*) (range)	
	5–10	15–20	5–10	15–20
Parameter				
S_pO_2	90.3 ± 3.1 (13) (85–95)	90.6 ± 4.1 (14) (79–95)	84.5 ± 7.8 (14) (72–94)	86.9 ± 5.4 (15) (75–92)
Heart rate	66.6 ± 24.9 (16) (40–125)	66.6 ± 26.0 (15) (40–126)	65.5 ± 16.0 (16) (48–112)	65.9 ± 29.8 (16) (40–172)
Respiration rate	30.8 ± 22.3 (16) (11–102)	29.5 ± 27.3 (15) (9–112)	28.3 ± 22.5 (16) (8–102)	33.3 ± 30.5 (16) (8–122)
Rectal temperature (C)	41.1 ± 1.0 (16)[a] (39.3–42.2)	40.9 ± 1.2 (15) (39.0–42.2)	40.1 ± 1.1 (16) (38.5–42.2)	40.0 ± 1.1 (16) (38.6–42.2)

[a] Temperatures ≥ 42.2 C were recorded as 42.2 C.

($P<0.05$) in the second time period for C/X treated deer than for T/X treated deer.

Reversal times of C/X treated deer were rapid ($\bar{x}=1.9$ min.), compared to reversals of T/X treated deer ($\bar{x}=165.5$ min) (Table 1). Because of injection errors, two C/X treated deer did not receive the full subcutaneous dose of naltrexone and yohimbine; however, reversal times were typical (1.0 and 1.8 min), and there were no signs of narcotic recycling. Anesthetic recycling was not present after antagonist administration in any of the C/X treated deer; however, at least five of the 16 T/X treated deer were found partially or fully immobilized 1–4 hr after initial standing.

One C/X treated deer sustained a laceration on its leg, and another sustained a lower lip avulsion. Both recovered normally with only superficial treatments. One female injected with T/X, ate from a feeder located in the release pen before succumbing to drug effects and regurgitated while being carried to a stall. She died 3 wk later. Aspiration pneumonia was determined to be the probable cause of death. No other deer exhibited health complications within 1 mo post-treatment.

DISCUSSION

Short induction time is one of the most important characteristics of a remotely delivered immobilization drug. The risk of injury and hyperthermia increased with prolonged induction times. In field situations, long induction times increase flight distance and reduce the chance of recovering an animal (Ryeng, 2001).

Jessup et al. (1984) reported a mean carfentanil dosage of 30.0 μg/kg was effective for remote immobilization of captive mule deer (*Odocoileus hemionus*), and Caulkett et al. (2000) reported an IM injection of 10.0 μg/kg carfentanil was effective for immobilizing captive mule deer and mule deer×white-tailed deer hybrids. However, we determined that 1.2 mg of carfentanil (17.8–29.0 μg/kg) combined with 10.0 mg of xylazine (0.15–0.24 mg/kg) was not a reliable dose for producing short induction times and satisfactory immobilization in captive white-tailed deer. Furthermore, induction times did not dramatically decrease with higher carfentanil dosages and Haigh (1990) reported there is an increased risk of narcotic recycling with high dosages of ultra-potent opioids.

Not all field procedures would be possible when using the tested dosages of C/X as an immobilization drug combination for white-tailed deer because of variability of drug effect. The level of immobilization in all C/X treated deer was adequate for minimal handling; however, complex or invasive procedures would not have been possible in some individuals.

Safe chemical immobilization should minimize adverse effects to normal physiologic function. Respiratory depression is a concern with a combination of an opioid and xylazine (Klein and Klide, 1989; Haigh, 1990). However, hemoglobin saturation of C/X treated deer was greater than in T/X treated deer in the second time period and approached significance ($P=0.07$) for the first time period. Hyperthermia was common in C/X treated deer. Thus, C/X should only be used at this dose to immobilize white-tailed deer if adequate means to decrease body temperature are available.

Jessup et al. (1984) reported that rectal temperatures, heart rate, respiration rate, and blood pressure of a mule deer increased to unsafe levels as duration of carfentanil immobilization increased. Because some deer immobilized in the field are not recovered, we investigated the relationships between certain physiologic parameters and duration of immobilization. Because no relationship was found between heart rates or respiration rates and duration of immobilization, and rectal temperatures returned to normal as duration of immobilization increased, the recovery from C/X immobilization without reversal does not appear to increase the risks associated with carfentanil use in white-tailed deer.

Immobilization with C/X is effectively

and rapidly reversed using naltrexone and yohimbine in white-tailed deer. Deer were alert and fully coordinated within minutes of antagonist administration, with little risk of renarcotization. This ability to completely reverse immobilization may be extremely beneficial in field situations if deer react similar to the deer treated in the pen setting.

The T/X combination also effectively immobilized white-tailed deer. Induction times were rapid and immobilization was excellent for all individuals. In addition, all physiologic parameters remained satisfactory.

However, reversal times for deer immobilized with the combination of T/X were prolonged. The sluggish and uncoordinated demeanor of deer 20–30 min after yohimbine administration suggested residual effects from xylazine and/or Telazol®. The 0.125 mg/kg yohimbine dosage recommended by Kreeger (1996) may have been insufficient to antagonize the effects of xylazine when administered half IV and half SC. However, residual Telazol® effects may have also contributed to the long reversal times.

Costs to immobilize deer with 1.2 mg of carfentanil and 10 mg of xylazine were $15.05 per individual. Reversal using 120 mg of naltrexone and 6.5 mg of yohimbine was $23.33 per individual. Therefore, total cost per deer was $38.38.

Immobilization cost with 230 mg of Telazol® and 120 mg of xylazine was $12.08 per individual. Reversal with 6.5 mg of yohimbine was $2.93 per individual. Therefore, total cost was $15.01 per deer.

Although use of C/X to immobilize deer, and its reversal with naltrexone and yohimbine, was more costly than the other treatment, the ability to rapidly reverse the immobilization may increase the number of possible immobilizations each day and reduce overall costs.

Major disadvantages for the use of carfentanil are its risk to human personnel and its classification as a Schedule II narcotic. Carfentanil is extremely toxic to humans and should never be used in the absence of a syringe containing an emergency antagonist. As an added precaution, we also had Emergency Medical Technicians present during our treatment of deer. All ultra-potent opioids are classified as Schedule II narcotics that require strict license and usage requirements overseen by the United States Drug Enforcement Administration.

Additional dose evaluations of carfentanil and xylazine should be conducted to reduce induction times and improve reliability of anesthesia in white-tailed deer. Furthermore, research of yohimbine and other alpha-$_2$ antagonists and benzodiazepine antagonists should be conducted to decrease the long recovery times associated with T/X.

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