Dexmedetomidine-Tiletamine-Zolazepam Followed by Inhalant Anesthesia in Spectacled Bears (Tremarctos ornatus)

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ABSTRACT

Background: The spectacled bear (Tremarctos ornatus) is the only bear species inhabiting South America and is classified as vulnerable according to the International Union for Conservation of Nature (IUCN) Red List of Threatened Species. Among the few publications on the use of general anesthesia and advanced monitoring of ursids in veterinary hospital settings, little is described regarding chemical restraint, general anesthesia and monitoring of spectacled bears. This case series describes the use of a dexmedetomidine-tiletamine-zolazepam chemical restraint combination and its effects on cardiorespiratory variables and arterial blood gases observed in two spectacled bears undergoing isoflurane anesthesia for imaging and/or surgical procedures.

Cases: Two female, one adult and one senile, all-term captive spectacled bears were referred to the Veterinary Teaching Hospital at the Universidade Estadual Paulista - Unesp, Botucatu campus, both with a presumable history of recent trauma. After immobilization with an intramuscular (IM) administration of tiletamine-zolazepam (3.8 - 4.3 mg/kg) and dexmedetomidine (6.4 - 7.6 µg/kg), induction of anesthesia was achieved by means of intravenous (IV) propofol (1 - 2 mg/kg). After orotracheal intubation animals underwent isoflurane anesthesia under mechanical ventilation through the remainder of the procedures. Initial settings of inspiratory flow rate were adjusted to obtain peak airway pressure (P\textsubscript{peak}) of 10 cmH\textsubscript{2}O and tidal volumes (V\text{t}) of 10 mL/kg, as well as respiratory rates (f\text{R}) and inspiration-to-expiration (I:E) ratio of 10 breaths/min and 1:2, respectively, and were then adjusted throughout anesthesia to maintain normocapnia (end-tidal carbon dioxide concentrations between 35 and 45 mmHg). One of the individuals was chemically restrained (6.4 mg/kg of tiletamine-zolazepam and 7.7 µg/kg of dexmedetomidine) on a second anesthetic event for imaging procedures. Arterial blood gas analysis were performed with animals breathing room air and oxygen-enriched air. Both animals exhibited severe hypoxemia (partial pressure of oxygen [PaO\textsubscript{2}] < 60 mmHg) while breathing room air (inspired oxygen fraction [FiO\textsubscript{2}] ≅ 0.21). An impaired blood oxygenation (PaO\textsubscript{2}/FiO\textsubscript{2} < 400) was still observed despite mechanical ventilation and the provision of 1.0 FiO\textsubscript{2}. Alveolar recruitment maneuvers (3 sequential mechanical sights with P\textsubscript{peak} at 20 - 30 cmH\textsubscript{2}O during 15 - 30 s each) were then performed, which resulted in improved PaO\textsubscript{2}/FiO\textsubscript{2} ratios. All other blood gas, electrolytes and acid-base variables did not appear to be importantly altered by chemical restraint and general anesthesia.

Discussion: In spite of severe hypoxemia recorded in animals breathing room air, dexmedetomidine-tiletamine-zolazepam resulted in reliable chemical restraints and is a feasible option for immobilizing spectacled bears. Hypoxemia is the most commonly described complication in bear anesthesia, and was also evidenced in the present report. However, low PaO\textsubscript{2}/FiO\textsubscript{2} ratios tend to be paralleled by hypoventilation and therefore counteracted by oxygen supplementation in bears, which was not observed in the present report. In fact, blood oxygenation only reached acceptable values after alveolar recruitment maneuvers, which is compatible with an atelectasis-related hypoxemia. Ideally, inhalant anesthesia or field chemical restraint should be accompanied by advanced monitoring (cardiorespiratory variables and blood gas analysis) until further studies address the management of hypoxemia in spectacled bear. Advanced monitoring was of major importance for a safe outcome and an uneventful recovery in this species.

Keywords: balanced anesthesia, general anesthesia, spectacled bear, Tremarctos ornatus, wildlife.
INTRODUCTION

The spectacled bear (Tremarctos ornatus), also known as Andean bear, is the only extant ursid species endemic to South America and is typically found along the Andes Mountains [26]. In spite of its wide habitat range, the species is classified as “vulnerable” regarding its global extinction risk, since habitat encroachment, climate change and the expansion of road systems have altogether fragmented the spectacled bear’s territory and reduced its abundance [26].

All bear species must undergo chemical restraint followed or not by general anesthesia for wildlife management or for ordinary care in zoo practices [5]. Likewise the majority of wild species, the scientific literature on bear anesthesia has mainly focused on describing out-of-hospital chemical restraint protocols for non-invasive procedures [2-7,10-13,22,25], with few studies addressing general anesthesia and advanced monitoring in ursids [15,20,24]. Although chemical immobilization has been described for polar [2], brown [3,5,10-13,25], black [4,7], and sun bears [22], anesthesia in Tremarctos ornatus is still in its infancy [20]. Inasmuch as the threats to native populations of spectacled bears have grown in recent years, there is an increased need to develop safe anesthetic combinations and monitoring in this species. The purpose of this report is to describe the chemical restraint and the cardiorespiratory changes recorded during inhalant anesthesia in two spectacled bears.

CASES

Case 1. An 8-year-old adult female spectacled bear (Tremarctos ornatus), inhabitant of the Zoological Park “Quinzinho de Barros” (Sorocaba, São Paulo, Brazil), was found limping and was referred to the Veterinary Medical and Research Centre in Wild Animals (CEMPAS) at the São Paulo State University (UNESP), School of Veterinary Medicine and Animal Science (Botucatu, SP, Brazil).

Upon admission, the animal showed lameness of the pelvic limb. Body weight was estimated at 90 kg and chemical immobilization was performed with intramuscular (IM) tiletamine-zolazepam1 combined with dexmedetomidine2 at target doses of 3 mg/kg and 5 µg/kg, respectively. A pressurized gas system using carbon dioxide deployed a dart at close range by means of a blowpipe. Complete immobilization was achieved within 10 minutes. After actual body weight was 70 kg, doses of tiletamine-zolazepam1 and dexmedetomidine2 effectively administered were 3.8 mg/kg and 6.4 µg/kg, respectively.

An 18 G intravenous (IV) catheter3 was aseptically inserted into the right saphenous vein before the animal was transferred to the surgical facility. Thirty seven min after blow darting, anesthesia was induced with IV propofol4 (2 mg/kg) and orotracheal intubation was performed with a 14.0 mm endotracheal tube5 upon direct visualization of the larynx with a laryngoscope blade. The bear was positioned in lateral recumbency and anesthesia was maintained with isoflurane6 diluted in 1.0 inspired oxygen fraction (FiO2) at a flow rate of 50 mL/kg/min delivered through a circle breathing circuit. The vaporizer setting was initially adjusted to maintain immobility and prevent spontaneous breathing efforts during intermittent positive-pressure ventilation7. A lactated Ringer’s solution8 was administered at 5 mL/kg/h using a peristaltic pump9.

After the onset of mechanical ventilation, an arterial sample was obtained by puncture of the femoral artery to evaluate temperature-corrected blood gases and electrolytes10 [partial pressures of oxygen (PaO2) and carbon dioxide (PaCO2), pH, bicarbonate (HCO3-), extracellular base excess (BE ecf), anion gap (GAP), lactate, sodium (Na+), potassium (K+), chloride (Cl-) and hematocrit (Ht)]. Twenty min after propofol administration, mild acidosis and a significantly low PaO2/FiO2 ratio (below 200) were observed (Table 1). An alveolar recruitment maneuver was then performed (3 sequential mechanical sights with peak airway pressure [Ppeak] at 20 - 30 cmH2O during 15 - 30 s each).

Cardiorespiratory variables were recorded by a multiparameter monitor11 at 5 min intervals throughout anesthesia. Although under continuous cardiorespiratory monitoring, the first set of physiological data was recorded only 50 min after darting, because of the time spent transferring the patient to the operating room. A pulse oximeter probe placed on the tongue recorded hemoglobin peripheral oxygen saturation (SpO2). A multi-gas analyzer was connected to the Y-piece of the breathing circuit for continuous measurement of end-tidal carbon dioxide (ETCO2) and end-tidal isoflurane concentrations (ETiso) through a sidestream sampling line. Initial settings of inspiratory flow rate were adjusted to obtain Ppeak of 10 cmH2O and tidal volumes (Vt) of 10 mL/kg. Respiratory rate (fR) and
inspiration-to-expiration (I:E) ratio were initially set at 10 breaths/min and 1:2, respectively, and were then adjusted throughout anesthesia to maintain ETCO₂ between 35 - 45 mmHg.

Heart rate (HR) and rhythm were also recorded (lead II electrocardiogram). Core temperature was monitored by an esophageal sensor and maintained above 36.5°C by means of a forced warm air device. Additionally, the right dorsal pedal artery was aseptically catheterized with a 20 G catheter and connected via a noncompliant tubing to a pressure transducer system filled with heparinized (5 IU/mL) physiological saline to measure systolic, diastolic and mean arterial blood pressures (SAP, DAP and MAP, respectively). The arterial catheter was also used to collect samples for blood gas and electrolyte analysis throughout anesthesia (Figure 1). Although the first recruitment maneuver improved the PaO₂/FiO₂ ratio from 92 to 260 (Table 1) at 46 min of inhalant anesthesia, it remained below normal limits (400), therefore this maneuver was repeated. The third arterial blood sample was collected 120 min after the onset of anesthesia and revealed a normal PaO₂/FiO₂ ratio, therefore an oxygen-air mixture (FiO₂ ≅ 0.6) was thereafter delivered throughout the remainder of the procedure (Table 1).

Radiography revealed a tibial fracture and an osteosynthesis was performed with an intramedullary pin and a plate-rod fixation. With the aim of providing intraoperative analgesia, a combined sciatic and femoral nerve blocks (ScFeNB) were performed under ultrasound guidance in B-Mode with a 7.5 MHz linear array transducer. Both techniques were accomplished by insertion of a 160 x 2 mm Klein cannula and were adapted from recommendations in dogs [18]. Briefly, the sciatic nerve was approached in the middle third of thigh with the transducer positioned perpendicular to the long axis of the pelvic limb, caudal to the femur. The sciatic nerve was identified between the fascia of the biceps femoris and abductor muscles. At this site, a combination of 2% lidocaine (2.8 mg/kg) and 0.5% bupivacaine (0.7 mg/kg) was administered (total volume: 0.3 mL/kg). The femoral nerve blockade required a medial approach to the thigh (just above the femoral triangle), where a transverse image of the femoral artery, vein and nerve were obtained. This site received 0.1 mL/kg of the 1:1 mixture of lidocaine (1 mg/kg) and bupivacaine (0.25 mg/kg). For additional analgesia, IV morphine (0.1 mg/kg) and IV meloxicam (0.1 mg/kg) were also administered.

Adjustments in ventilator resulted in ETCO₂ between 33 and 48 mmHg. No arrhythmias were noticed and SpO₂ remained above 95%. Direct blood pressure and HR were stable during the first hour of surgery, but gradually increased from that point onwards. The ETISO₂ was progressively increased after 1 h of surgery by adjusting vaporizer settings to control the sympathetic response to surgical stimulation (Table 2). At the end of surgery, the patient was weaned from the ventilator by stepwise reducing P_peak and f_next until spontaneous respiratory efforts were evident on the capnographic waveform. Extubation was performed upon recovery of the swallowing and palpebral reflexes. Recovery from anesthesia was uneventful. Immediate postoperative pain assessment showed no signs of discomfort and no rescue analgesics were administered at this time point.

The bear was anesthetized a month later for surgical follow-up with tiletamine-zolazepam and dexmedetomidine (6.4 mg/kg and 7.7 µg/kg, respectively). Total dosages of drugs were higher than previously used in this animal because of poor dart placement. An arterial blood gas sample collected while the animal was breathing room air again showed mild acidosis and
severe hypoxemia (Table 1). Because of the short time required for immobilization and rapid onset of recovery the animal did not receive supplemental oxygen.

**Case 2.** A 27-year-old senile female spectacled bear, from the “São Carlos Ecological Park” (São Carlos, São Paulo, Brazil) was admitted to the Veterinary Hospital because of a functional impotence of the right thoracic limb. Body weight was estimated at 60 kg and the animal was blowpipe-darted with tiletamine-zolazepam and dexmedetomidine mixture at target doses of 3 mg/kg and 5 µg/kg, respectively. The bear briskly moved just prior to injection, which led to dart misplacement. Fifteen min later, the bear was not recumbent and approaching the animal was judged unsafe. Supplemental doses of tiletamine-zolazepam and dexmedetomidine were 4.3 mg/kg and 7.6 µg/kg, respectively.

While the animal was breathing room air, an arterial blood sample was collected by puncture of the femoral artery for blood gas and electrolyte analysis. All variables showed unremarkable changes, except for a severe hypoxemia (PaO₂ < 60 mmHg) [Table 1]. In order to provide cardiorespiratory support and because a long period of immobilization was anticipated for diagnostic procedures, the animal underwent general anesthesia. Firstly, an 18G IV catheter was inserted into the right saphenous vein. General anesthesia was induced with IV propofol (1 mg/kg) and orotracheal intubation was performed exactly as described in Case 1 (Figure 2). Anesthesia was maintained with isoflurane in oxygen (FiO₂: 1.0; oxygen flow rate: 50 mL/kg/min) delivered through a circle breathing circuit. Mechanical ventilation settings and monitored physiological variables followed the same pattern of Case 1. A lactated Ringer’s solution was administered at 10 mL/kg/h using a peristaltic pump because the patient was mildly

### Table 1. Temperature (°C) corrected partial pressures of oxygen (PaO₂) and carbon dioxide (PaCO₂), pH, bicarbonate (HCO₃⁻), base excess of extracellular fluid (BEecf), anion gap (AG), lactate, sodium (Na⁺), potassium (K⁺), chloride (Cl⁻) and hematocrit (Ht) obtained either by puncture of the femoral artery or by the arterial line placed within the dorsal pedal artery of two spectacled bears submitted to different inspired oxygen fractions (FiO₂).

| Variable       | Bear 1         | Catheter | Bear 1*      | Catheter | Bear 2  | Catheter |
|----------------|----------------|----------|--------------|----------|---------|----------|
| Temperature (°C) | 37.8           | 37.3     | 36.8         | 36.5     | 36.9    | -        |
| ≈ FiO₂ (%)     | 1.0            | 1.0      | 1.0          | 0.6      | 0.6     | 0.21     |
| PaO₂ (mmHg)    | 92             | 260      | 494          | 363      | 309     | 42       |
| PaO₂/FiO₂      | 92²            | 260³     | 494³         | 605³     | 515³    | 200      |
| PaCO₂ (mmHg)   | 40.7           | 40       | 46.1         | 44.8     | 46      | 45.6     |
| pH             | 7.32           | 7.32     | 7.30         | 7.30     | 7.31    | 7.28     |
| HCO₃⁻ (mmol/L) | 20.1           | 20       | 22.1         | 21.6     | 22.3    | 20.6     |
| BEecf (mmol/L) | -4.8           | -5.0     | -3.4         | -3.9     | -3.1    | -5.0     |
| AG (mmol/L)    | 17.4           | 18       | 16.7         | 16.7     | 16.6    | 20.4     |
| Lactate (mmol/L) | 0.4            | 0.2      | 0.1          | 0.3      | 0.2     | 0.7      |
| Na⁺ (mmol/L)   | 149            | 151      | 146          | 148      | 149     | 143      |
| K⁺ (mmol/L)    | 3.20           | 3.12     | 3.60         | 3.47     | 3.77    | 3.58     |
| Cl⁻ (mmol/L)   | 111            | 113      | 107          | 110      | 110     | 102      |
| Ht (%)         | 43             | 38       | 36           | 36       | 36      | 42       |

*Second anesthetic procedure of Case 1 bear. †After the onset of oxygen supplementation and mechanical ventilation. ‡After the first recruitment maneuver. ††Before oxygen supplementation and mechanical ventilation.

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dehydrated (estimated 5% dehydration). Intravenous methadone (0.1 mg/kg) and meloxicam (0.1 mg/kg) were also provided for analgesia.

The ETISO was maintained at 1.1 - 1.7% throughout the procedure. The ventilator settings resulted in ETCO₂ values ranging from 30 - 35 mmHg. Pulse oximetry, HR and arterial pressure were stable throughout anesthesia (Table 2). A second arterial blood sample collected from the arterial catheter 60 min after induction of anesthesia showed a relatively low PaO₂/FiO₂ ratio (Table 1) and the same recruitment maneuver described for Case 1 was performed.

At the end of the imaging procedures, isoflurane was discontinued (90 min after induction of anesthesia). The animal was weaned from mechanical ventilation and extubated as described in Case 1. The bear was conducted to its enclosure and recovery was uneventful.

**DISCUSSION**

Immobilization with tiletamine-zolazepam and dexmedetomidine was smooth and recumbency was achieved within 10 min of the last darting in both cases. Although vomiting, hypersalivation and seizure-like episodes are common complications in bear anesthesia [5,6,10,22,25], these were not observed in the present report. The combination of tiletamine-zolazepam and dexmedetomidine at the doses of this report provided good muscle relaxation and allowed safe handling the bears. The onset of immobilization from the last darting (< 10 min) was similar to that reported for spectacled bears anesthetized with tiletamine-zolazepam-metadomidine (8 min) [20]. Brief onsets of immobilization augment the safety of wildlife procedures because it enables an early approach and anesthetic monitoring [1].

Dexmedetomidine probably improved muscle relaxation and reduced tiletamine-zolazepam requirements for immobilization, since doses were at least twice as low in comparison to doses of tiletamine-zolazepam alone described in captive [2] and in free-ranging bears [3]. A recent review on spectacled bear anesthesia revealed that tiletamine-zolazepam (1.5 mg/kg), ketamine (1.9 mg/kg) and medetomidine (15 µg/kg) were the most commonly reported combinations for chemical restraint, yet 48% of animals required supplemental injections for proper immobilization [20]. Despite the higher doses of tiletamine-zolazepam reported here (mean 4.1 mg/kg), the combination with dexmedetomidine resulted in a reliable chemical restraint without adverse effects. Dexmedetomidine doses were within the range of those reported for other bear species [7,10,25]. The chemical restraint protocol at dosages reported here could be used for minor procedures in zoo practices or as premedication for general anesthesia in captive *T. ornatus*. However, higher dosages may be necessary under conditions of fieldwork [2]. Because general anesthesia was promptly induced after chemical immobilization, the total time of workable immobilization was unknown.

As opposed to bilateral motor blockade of the pelvic limbs produced by neuraxial anesthesia (e.g., epidural anesthesia), wildlife can benefit from unilateral blockade of the pelvic limbs produced by regional techniques because animals are able to rapidly regain standing position, reducing the stress during early postoperative period [8]. The ScFeNB technique was executed because of its indications for perioperative analgesia and isoflurane-sparing effects. The trend for an increase in HR and arterial blood pressure after the first hour of surgery (Case 1) could have been triggered by the transiently inadvertent intra-articular position of the intramedullary pin at the stifle joint. The innervation of the canine stifle involves multiple nerve components (e.g., sciatic, femoral, obturator, lateral femoral cutaneous nerves), therefore the ScFeNB alone might have been insufficient to induce complete desensitization of the stifle joint [9]. Another possibility is that the sciatic nerve was only partially blocked in view of the thick layer of adipose tissue of the thigh. Furthermore, the technique was oriented by guidelines available for small animals [23], while anatomical structures and landmarks may vary among species. Nevertheless, the ultrasound-guided ScFeNB showed promising results as
most of the surgical procedure was accomplished under hemodynamic stability and low isoflurane requirements. To the authors’ knowledge, this is the first description of the applicability of ultrasound guided regional anesthesia in a bear.

Hypertension and bradycardia are common findings during early phases of anesthesia with tiletamine-zolazepam combined with alpha2-agonist agents in ursids [10,25]. Transient hypertension is caused by increases in peripheral vascular tone, leading to baroreceptor mediated decreases in HR and cardiac output [17]. However, MAP remained within normal ranges for the most part of anesthesia (between 60 and 100 mmHg) (Table 2) and dexmedetomidine-induced hypertension was not detected during the first hour of maintenance of anesthesia with isoflurane because the alpha-2 agonist-related vasoconstriction is transient and isoflurane has vasodilating properties. When hypertension (MAP > 100 mmHg) was observed after 1 hour of anesthesia in Case 1, it was likely because of sympathetic stimulation caused by surgical stimulation.

Although direct arterial blood pressure measurements have been described for bears [2,25], arterial lines are usually placed in the femoral artery, which poses an inherent risk for bleeding and hematoma formation. Catheterization of the dorsal pedal artery is common practice in small animal anesthesia [14] and appeared to be a feasible option for spectacled bears.

It is challenging to determine whether the chemical restraint protocol caused bradycardia given the absence of physiological HR values for *Tremarctos ornatus*. Dexmedetomidine-premedicated captive Asiatic black bears showed similar HR values (66 bpm) [7] in comparison to the spectacled bears of this report (70 bpm), whereas grizzly bears are considered to present bradycardia at HR below 50 bpm [10]. Spectacled bears under tiletamine-zolazepam-based protocols also exhibited HR values in a similar range to that observed in the present report (64 - 71 bpm)[20]. One should note that cardiovascular variables were first recorded approximately 50 min following initial darting. Therefore, it is likely that the effects of dexmedetomidine had weaned off considering its plasma half-life in dogs [16]. For this reason, the typical bradycardia and hypertension observed during early stages of the alpha2-agonist sedation might have been unnoticed.

Hypoxemia (PaO2 < 80 mmHg) is the most common complication in bear anesthesia under field conditions, where oxygen supplementation could be limited [2,7,12,20,24]. In order to evaluate oxygenation, not only SpO2 and PaO2 should be assessed, but also the PaO2/FiO2 ratio. Under normal conditions, the PaO2/FiO2 ratio should be above 400 mmHg [18]. Despite the fact that both bears exhibited impaired oxygenation at the time of the first arterial blood gas sample, the PaO2/FiO2 ratio indicated an important oxygenation impairment only in Case 1, while in Case 2 the oxygenation was only moderately compromised. An arterial blood sample in Case 1 was not drawn when the animal was breathing room air before the onset of general anesthesia; yet a severe hypoxemia (PaO2 42 mmHg) was observed a week later when the bear was immobilized by the same drug combination while breathing room air (Table 1).

### Table 2. Range of heart rate (HR), arterial blood pressure (systolic [SAP], diastolic [DAP] and mean [MAP]), end-tidal carbon dioxide (ETCO2), end-tidal isoflurane (ETiso) and peripheral oxygen saturation of hemoglobin (SpO2) recorded in two isoflurane-anesthetized spectacled bears under mechanical ventilation.

| Variable     | Bear 1 (< 1 h) | Bear 1 (> 1 h) | Bear 2 |
|--------------|----------------|----------------|--------|
| HR (beats/min) | 65 - 75 | 85 - 105 | 65 - 75 |
| SAP (mmHg)    | 90 - 105 | 120 - 175 | 85 - 110 |
| DAP (mmHg)    | 60 - 75 | 75 - 110 | 50 - 65 |
| MAP (mmHg)    | 67 - 80 | 85 - 135 | 63 - 77 |
| ETCO2 (mmHg)  | 33 - 40 | 38 - 48 | 30 - 35 |
| ETiso (%)     | 1.3 - 1.9 | 1.9 - 2.6 | 1.1 - 1.7 |
| SpO2 (%)      | > 90 | > 90 | > 90 |
Considering that PaCO₂ was within normal ranges (Table 2), hypoventilation had no impact on oxygen exchange. For this reason, it was decided to perform an alveolar recruitment maneuver in both bears, following recommendations in horses under atelectasis-related hypoxemia [21]. In fact, right-to-left pulmonary shunt is an important source of oxygenation impairment in anesthetized horses [19]. Spectacled bears are medium-sized animals (approximately 100 kg) and intrapulmonary shunting due to atelectasis related to recumbency could have contributed to impaired oxygenation, since the PaO₂/FiO₂ ratio was increased after the recruitment maneuver (Case 1). In light of the potential risks for alveolar collapse and perpetuation of intrapulmonary shunt when providing 100% oxygen to 0.6 after an improvement in PaO₂/FiO₂ ratio was observed.

Given the paucity of information on spectacled bear anesthesia, this case report should aid wildlife veterinarians in the anesthetic management of such species. The dosages of drugs used in the present report may be a reference for chemical restraint in *Tremarctos ornatus*, as effective dosages may vary among species [2,3]. The need for close cardiorespiratory and arterial blood gas monitoring should be emphasized. Ultimately, oxygen supplementation and ventilatory support should be available to counteract hypoxemia.

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