Tea tree oil, also known as Australian tree tea oil or melaleuca oil, is obtained by steam distillation of the freshly harvested leaves of *Melaleuca alternifolia* trees. Approximately 2% of the weight of the leaves can be harvested as oil. The tree is native to Spain, Portugal, and Australia and has been introduced to the southern United States, especially Florida. Tea tree oil is a complex mixture of approximately 100 components. This mixture has terpene-like odor, is colorless or pale yellow, and consists of 50% to 60% terpenes of various types, mainly cymene, terpinene, pinene, cineole, and higher alcohols.

Tea tree oil is known to have bactericidal and fungicidal properties and is used topically in humans and other animals for various skin conditions such as acne, boils, burns, corns, gingivitis, herpesvirus infections, impetigo, insect bites, lice, oral ulcers, miliaria, dermatophytosis, skin and vaginal infections, oral candidiasis, and tonsillitis. The oil has been added to baths or vaporizers to help treat respiratory tract disorders. It has also been used in perfumes and aromatherapy. It is marketed in toothpaste, soap, lotion, and skin cream. The oil is marketed in health food stores as an antiseptic, fungicide, and skin care agent. Internal use has also been recommended by herbalists for the treatment of parasitic diseases, and inhalation of TTO in steam has been recommended for the treatment of sinus and throat infections. In the early 1900s, TTO was used in surgery and dentistry and for skin injuries.

In veterinary medicine, TTO is marketed for use on dogs, cats, ferrets, and horses for cleaning hair, healing hotspots, and treating some skin allergies. The concentration of TTO used in most skin care products is low and may vary from 0.1% to 1.0%. Undiluted TTO can be used topically in humans by most individuals without adverse effects. Animal owners sometimes knowingly or accidentally use 100% TTO to treat various skin conditions in their dog or cat. Despite its widespread availability and use, there is a paucity of safety and toxicosis information about TTO in dogs and cats. The purpose of the study reported here was to review toxicosis incidents resulting from the use of 100% TTO in dogs and cats reported to the ASPCA APCC from January 2002 to December 2012, focusing on clinical signs (onset time, types, frequency, duration, and severity), epidemiological information, and treatment.

### Materials and Methods

#### Criteria for case selection
Clinical data involving exposure to 100% TTO from January 1, 2002, to December...
SMALL ANIMALS

November 31, 2012, were retrieved from the APCC electronic medical record database. The APCC provides a 24-hour telephone consulting service to support animal owners and veterinarians with the diagnosis and treatment of animal poisoning cases throughout the United States and Canada. Only dog and cat incidents involving an acute exposure to 100% TTO alone were included in the study, and incidents involving exposures to diluted TTO or multiple agents were excluded. Furthermore, only incidents classified as toxicosis (high likelihood that the observed clinical signs were caused by TTO) or suspected toxicosis (medium likelihood that the observed clinical signs were caused by TTO) as assessed by an APCC veterinarian were included. These classifications by the APCC veterinary staff are assigned to each incident on the basis of history of exposure; type, onset time, and duration of clinical signs; information present in the literature; and previous experience dealing with the agent.

For each incident, the following information was retrieved: animal signalment (age, weight, sex, reproductive status, and breed); intent of use of TTO (intentional [the product was knowingly used for treatment purposes] vs accidental [the product was used accidentally]); approximate amount (milliliters) to which the animal was exposed; exposure certainty (observed [the exposure was witnessed] vs evidenced [there was conclusive evidence that an exposure occurred [eg, a chewed bottle with product missing] but it was not witnessed]); route of exposure (cutaneous, oral, both cutaneous and oral, or other); onset time (hours), types, and duration of clinical signs; CBC or serum biochemical changes if available; mortality rate; severity of illness (mild, moderate, or major illness); final outcome (recovered or died); and geographic location of the incident.

Mild illness was when the animal had clinical signs that were minimally bothersome and resolved quickly (eg, increased salivation or mild vomiting). Moderate illness was when the clinical signs were more pronounced, prolonged, or systemic in nature (eg, ataxia, weakness, or paresis). Major illness was when the animal had clinical effects deemed life-threatening (eg, coma, obtundation, or seizures). Dogs and cats were allocated into 5 age groups: neonate (0 to 9 days), infant (> 9 days to age at weaning), juvenile (greater than age at weaning to less than age at sexual maturity), adult (age at sexually maturity), and elderly (age > 80% of animal’s life expectancy).

Statistical analysis—Percentages were calculated for categorical variables (species, severity of illness, sex, and breed), and medians, means, and ranges were calculated for continuous variables (age and weight, both of which were skewed). Statistical analyses with \( \chi^2 \) testing were performed to compare severity of illness within species (cats or dogs) or between species as well as to measure the association between severity of illness and sex and breed. Nonparametric ANOVA (Kruskal-Wallis) was used to evaluate the relationship between severity of illness and age or weight. A Wilcoxon rank sum test with a Bonferroni correction was used for post hoc comparisons of significant ANOVA results. Values of \( P < 0.05 \) were considered significant.

Results

Overall data—During the 10-year study period, 443 dogs and cats were exposed to 100% TTO, including 337 (76%) dogs and 106 (24%) cats. The product was used intentionally for treatment purposes in 395 (89%) incidents, accidently in 9 (2%), and for unknown reasons in 39 (9%). Two hundred eight (47%) incidents were classified as toxicosis, and 135 (30%) were classified as suspected toxicosis. Exposure was observed in 310 of 443 (70%) animals and evidenced in 133 (30%). The route of exposure was known in 438 cases; exposure was cutaneous in 221 (50%), cutaneous and oral in 133 (30%), oral only in 67 (15%), aural in 16 (3.6%), and IV in 1. The severity of illness was classified as major in 31 (7%) incidents, moderate in 248 (56%), and mild in 161 (36%). A significant \( (P < 0.001) \) association was detected between the severity of illness and the species (dog vs cat) involved. Dogs were more likely to develop moderate illness, and cats were more likely to develop mild or major illness. Death was reported in 2 dogs. The geographic location of the exposure was known in 430 incidents. Incidents were reported from 41 states, the District of Columbia, and 4 Canadian provinces. The highest number of cases were from California (80 [19%]), followed by Florida (31 [7%]), New York (28 [7%]), Texas (23 [6%]), New Jersey (22 [5%]), Massachusetts (21 [5%]), and Pennsylvania (20 [5%]). The approximate amount used varied from 0.1 to 85 mL/animal and was not quantifiable (the amount used could not be determined) in 297 (67%) animals. Therefore, no further analyses were performed on dose amount and outcomes. Clinical signs of toxicosis were noticed within 2 to 12 hours after exposure and lasted up to 72 hours.

Dog incidents—The most commonly involved dog breeds were Labrador Retriever (25/337 [7%]), Yorkshire Terrier (19 [6%]), Pug (19 [6%]), Shih Tzu (17 [5%]), Chihuahua (16 [5%]), Bichon Frise (11 [3%]), and Boxer (11 [3%]). There were 162 (48%) male dogs and 175 (52%) female dogs. Reproductive status was known in 325 dogs; 124 (37%) were spayed females, 122 (36%) were neutered males, 28 (9%) were sexually intact males, 42 (13%) were sexually intact females, and 1 (0.3%) was a pregnant female. Age range was 0.1 to 15 years, with a median age of 3 years (mean, 4 years), and 7% of dogs were < 1 year of age. Weight range was 0.2 to 71 kg (0.44 to 156.2 lb), with a median of 10 kg (22 lb; mean, 16 kg [35.2 lb]). Outcome was known in 26 incidents; 24 (92%) dogs recovered with home treatment (bathing or monitoring), and 2 (8%) dogs recovered with veterinary care. The 2 deaths involved a 7.5-year-old neutered male Old English Sheepdog and a 15-year-old neutered male Miniature Poodle. The Old English Sheepdog was accidentally administered 0.3 to 0.4 mL of TTO IV. The dog immediately collapsed and was determined to be in cardiac arrest (asystole). Resuscitation efforts were unsuccessful. The Miniature Poodle was treated with approximately 28.5 mL of TTO applied topically once a day for 3 days for an unknown reason. After the third dose, the dog became ataxic and was taken to a veterinarian. The dog was bathed, given
IV fluid therapy, and monitored at an emergency clinic overnight. The dog appeared to recover and was released to the owner the next morning but died at home approximately 60 hours after the last exposure. In both death cases, no necropsy was performed and the cause of death remained unknown.

The severity of the toxicosis, based on clinical signs, was classified as major in 18 of 337 (5%) dogs, moderate in 215 (64%), and mild in 102 (30%). The most commonly reported clinical signs were signs of depression, lethargy, listlessness, somnolence, or appearing subdued in 181 (54%) dogs; paresis, weakness, or hind limb weakness in 150 (45%) dogs; ataxia in 144 (43%) dogs; muscle tremors and fasciculation in 34 (10%) dogs; vomiting in 20 (6%) dogs; coma, collapse, or recumbency in 15 (5%) dogs; dermatitis, pruritus, or rash in 13 (4%) dogs; stiffness in 11 (3%) dogs; increased salivation in 10 (3%) dogs, and high serum liver enzyme activities (alanine aminotransferase, alkaline phosphatase, or aspartate aminotransferase) in 6 (2%) dogs. Liver enzymes with high serum activities included alanine aminotransferase (range, 180 to 892 U/L; 1 to 40 hours after exposure), alkaline phosphatase (range, 300 to 803 U/L; 5.5 to 4 days after exposure), and aspartate transaminase (range, 168 to 201 U/L; 1 hour to 3 days after exposure). Major illness developed in 18 dogs, including 14 in the adult group, 3 in the juvenile group, and 1 in the elderly group. No significant association was detected between the severity of illness and sex (P = 0.36), breed (the 7 most common breeds with > 3% of dogs included were analyzed as separate categories, and all remaining breeds were grouped together; P = 0.62), age (P = 0.12), or weight (P = 0.33).

Cat incidents—The most commonly involved cat breeds were domestic short hair (75/106 [71%]) followed by domestic medium hair (12 [11%]) and domestic long hair (9 [8%]), and 10 cats were of nonspecific breeds. There were 59 (56%) female cats and 44 (42%) male cats. Reproduction status was known in 102 instances; 42 (41%) were spayed females, 35 (34%) were neutered males, 14 (14%) were sexually intact females, and 9 (8.8%) were sexually intact males. The age range was 5 weeks to 20 years, with a median of 4 years, and 29% of cats were < 1 year of age. The weight range was 0.2 to 9.5 kg (0.4 to 20.9 lb), with a median of 4 kg (8.8 lb; mean, 3 kg [6.6 lb]). Of 6 cats for which outcome was known, all 6 made a full recovery (3 were bathed and monitored at home, and 3 were bathed and treated with methocarbamol and IV administration of fluids and were monitored at a veterinary clinic).

The severity of toxicosis, based on clinical signs, was major illness in 13 (12%) cats, moderate illness in 33 (31%) cats, and mild illness in 59 (56%) cats. Significantly (P = 0.001) more cats developed minor illness such as increased salivation and major illness such as coma and obtundation. The most common clinical signs were increased salivation or drooling (47 [44%] cats); ataxia (24 [23%]); signs of depression, lethargy, or signs of listlessness (21 [20%]); coma, recumbency, unresponsiveness, unconsciousness, or a semicomatose state (17 [16%]); muscle tremors or fasciculation (10 [9%]); hypothermia (8 [8%]); and dermatitis, pruritus, or rash (2 [2%]). No deaths were reported. The 13 cats with major illness comprised 6 infants, 5 juveniles, and 2 adults. No significant association was detected between the severity of toxicosis and sex (P = 0.86) or breed (categorized as domestic shorthair, domestic medium hair, or domestic longhair combined and other breed; P = 0.48). The severity of illness was significantly associated with age (P = 0.001) and weight (P < 0.001), with the severity of signs being much worse for younger cats (juveniles and infants) and cats with a lighter body weight.

**Discussion**

Results of this study indicated that the use of plant-derived 100% TTO to treat various ailments including dermatologic conditions in dogs and cats can result in severe neurologic effects (paresis, ataxia, tremors, and coma) or death. A higher percentage of dogs developed moderate illness (ataxia and paresis), compared with cats. Significantly more cats developed minor illnesses such as increased salivation and major illnesses such as coma and obtundation. Results of other studies indicate that cutaneous exposure to terpene-containing essential oils can result in clinical signs similar to the signs in the present study, including ataxia, weakness, signs of CNS depression, and coma in dogs and cats.

Tea tree oil is a complex heterogeneous mixture, and depending on the environment (eg, temperature and moisture) and soil conditions of the plant, a considerable batch-to-batch variation in the composition of TTO can occur. To limit this variation, currently, a series of standards are in place for oil of Melaleuca terpinen-4-ol type, which set maximum or minimum concentrations for 14 components of the oil. According to these standards, terpinen-4-ol, the putative antimicrobial component, must comprise at least 30% of the oil and 1.8-cineole, reportedly a skin irritant, must not exceed 15%. Toxicity of TTO can vary because of variation in the composition. This may be attributable to different physicochemical properties of various terpenes in the TTO that result in variation in pharmacokinetics. Some pharmacokinetic data are available for various terpenes when administered individually, but no data are available for these terpenes used as a mixture. Reports in the literature do not describe individual components responsible for toxicosis. It was not determined whether the TTO products used on animals in this case series met international standards, although wide variations in signs of toxicosis that may have been attributable to different compositions, brands, or standards were not observed, perhaps because of the large sample size (443 animals).

The terpenes are rapidly absorbed orally and cutaneously because they are lipophilic. Absorption of terpenes and thus toxicosis can increase in animals with erythematous or irritated skin. In the present study, 50% of the incidents involved only a cutaneous exposure. Cutaneous reactions in humans caused by TTO can be attributed to skin irritation from concentrated oil or to an allergic reaction. Allergic reactions are rare and occur only in some susceptible individuals, possibly because of formation of oxidation products that develop during storage. In the present study, cutaneous effects manifested by dermatitis, pruritus, or rash...
were reported in 15 animals (2 cats and 13 dogs). In the present study, no suspected allergic-type reaction was described. In a laboratory setting, cutaneous toxicosis was not detected in rabbits after cutaneous exposure to 2 g of TTO/kg (0.9 g of TTO/lb) of body weight. In Australia, 100% TTO is categorized as a schedule 6 poison (moderate potential for causing harm) and requires distinctive packaging and a safety warning on the label. Therefore, 100% TTO in Australia is sold in child-resistant packaging and the label instructs users not to take it internally and to keep it out of reach of children. To the authors’ knowledge, no such label cautions are required in the United States or Canada, which could be 1 reason that a majority (89%) of pet owners in this study chose to use it on their pets, assuming it would be safe. There is also a common belief among pet owners that natural plant-derived products, including pesticides, are better and safer, compared with man-made synthetic products.

In 2003, the American Association of Poison Control Centers recorded 787 exposures to TTO in humans; 318 of these were in humans < 6 years of age, 57 in those 6 to 19 years of age, and 212 in those > 19 years of age. The exposure was unintentional in 737 incidents and intentional in 20 incidents. The case outcome was known in 385 incidents; 238 people had no clinical signs, 134 had minor effects (skin irritation), 12 had moderate effects, and 1 had major effects. No deaths were reported. On the basis of 3 additional cases, the effect of TTO in children appears to be more severe (ataxia or unconsciousness) than in adults, probably the effect of TTO in children appears to be more severe.

In the present study, the majority of animals (395/443 [89%]) were exposed to TTO intentionally by the pet owner. The outcome information in the present study, when available, indicated that 24 of 26 dogs and 3 of 6 cats recovered with home treatment. Outcome information was not available for most exposures in this study, although the callers were instructed to call back if clinical signs continued or got worse. In the present study, although there was no significant association between age or weight and severity of illness in dogs, younger cats and cats with lighter weight did develop more severe signs.

Oral administration of 100% TTO has caused toxicosis in rats, rabbits, and humans. The oral LD_{50} in rats is 1.9 to 2.6 mL/kg (0.86 to 1.2 mL/lb). When administered 100% TTO orally at 1.5 mL/kg (0.68 mL/lb), rats developed lethargy, ataxia, and decreased activity within 72 hours. In the present study, clinical signs were noticed in dogs and cats within 2 to 12 hours and lasted for up to 72 hours.

The terpenes are predominantly metabolized in the liver by cytochrome P450-dependent monooxygenases and by conjugation with glucuronide and glycine. Because of this, hepatic insufficiency may predispose animals to toxicosis. Some terpenes may undergo enterohepatic recirculation, which may account for a longer duration of clinical signs (up to 72 hours) seen in some cases. Terpenes are excreted in the urine and feces. Approximately 60% to 80% of terpene metabolites are excreted in the urine 2 to 3 days after exposure.

In 1 clinical case, increased serum alanine aminotransferase and aspartate aminotransferase activities were reported in 3 cats that had been treated with a product containing 100% TTO. Two 28.5-mL bottles of the product were applied directly to the skin of the 3 cats. In the present study, 6 (2%) dogs had high serum activities of liver enzymes. Interestingly, no liver enzyme activity abnormalities were reported in cats. However, because serum biochemical analyses were not performed for all animals in this study, some abnormalities may have gone unreported.

Because of their limited ability to perform glucuronide conjugation, cats might be more susceptible to TTO toxicosis. In the present study, cats developed signs consistent with major illness in 12% of incidents and dogs developed major illness in only 5% of incidents, and this difference was significant. Cats also had significantly more clinical signs consistent with mild illness (56%), compared with dogs (30%). Because of their grooming behavior, cats are more likely to ingest TTO applied topically, compared with dogs. In the present study, increased salivation, most likely from ingestion of TTO through grooming, was the most common clinical sign in cats (44%), whereas only 3% of dogs developed that clinical sign. Younger cats (29% were < 1 year of age) had significantly higher prevalence of major effects from TTO, compared with adult and elderly cats. The exact reason for this was not apparent, but age and weight were moderately correlated. Therefore, this finding could be attributable in part to the lower body mass of younger cats, similar to children who are reportedly more susceptible to the effect of TTO. The other possible reason is reduced metabolic capacity in neonatal, infant, and juvenile animals, compared with adults, involving both phase I reactions (oxidation, reduction, and hydrolysis) and phase II reactions (conjugation reactions with glutathione, cysteine, glycine, and glucoronidation). For example, neonatal puppies may not have metabolic activity involving phase I reactions until they are 9 days of age and cytochrome P450 activity does not reach peak adult activity until 135 to 145 days of age. Eleven of 13 cats with major illness in this case series were infants (n = 6) or juveniles (5); however, no significant susceptibility of infant or juvenile cats was noted.

Treatment of TTO toxicosis consists of stabilization of CNS signs (tremors, shaking, and ataxia), skin decontamination with a dishwashing detergent, and supportive care with IV fluid therapy. In the present study, animals with mild effects were treated at home by bathing in a dishwashing liquid with further monitoring for the development of CNS signs (paresis, ataxia, and tremors).

Animals with moderate to major clinical effects should be assessed and treated at a veterinary facility. In stable patients, cutaneous exposures can be treated with a mild dishwashing detergent, soap, or nonsepticidal shampoo to remove remaining product from the skin and prevent additional absorption through the skin or orally through grooming, particularly in cats. To prevent further development of major signs (eg, coma or recumbency), tremors or muscle fasciculation should be treated first before bathing. Body tem-
Temperature should be monitored and corrected as needed with heating pads in patients with hypothermia.

With oral exposure, induction of emesis is not recommended because animals that already have developed neurologic effects have increased risk of aspiration, and risk of aspiration is also high because essential oils, including TTO, are of high viscosity and contain volatile hydrocarbons. Activated charcoal (1 to 4 g/kg [0.45 to 1.8 g/lb], made into a slurry in water and given with a stomach tube) can be administered after an oral TTO exposure and may bind terpenes and prevent further absorption, although its effectiveness is not known. To prevent regurgitation and aspiration, vomiting should first be controlled with maropitant (1 mg/kg, SC, q 24 h) before giving activated charcoal. Because of increased risk of aspiration, activated charcoal is not recommended in patients that are recumbent or comatose. Administration of fluids IV can correct dehydration and possibly aid in metabolite elimination. Muscle fasciculation or tremors can be treated with methocarbamol (25 to 50 mg/kg [11.4 to 22.7 mg/lb], IV, as needed; maximum dose, 330 mg/kg/d [150 mg/lb/d]) or diazepam (0.5 to 1.0 mg/kg, IV, as needed).6,12

Because of the risk for liver damage from terpenes in the TTO, animals with moderate to major clinical signs may require monitoring of liver enzyme activities for several days. Liver protectants such as S-adenosylmethionine (20 mg/kg/d [9.0 mg/lb/d], PO) or silymarin (20 to 50 mg/kg/d, PO) may be considered for such patients for 2 weeks. Other signs such as skin rashes or pruritus should be treated with antihistamines or corticosteroids.

Results of the study reported here indicated that use of 100% TTO in dogs or cats to treat various health conditions can lead to serious clinical signs, including signs of CNS depression, paresis, ataxia, and muscle tremors. Younger and smaller body weight cats are at greater risk of developing major clinical effects from TTO. Until more studies are available to determine the safety and efficacy of 100% TTO, its use in dogs or cats is not recommended.

References