

PEER-REVIEWED

# Marijuana exposure in animals

Caroline W. Donaldson, DVM

**M**arijuana, made from the dried leaves and flowers of the hemp plant (*Cannabis sativa*), is a commonly used recreational drug in people. It is a Schedule I controlled substance under the Controlled Substances Act. The pure form of marijuana's active ingredient, delta 9-tetrahydrocannabinol (THC), is available as dronabinol; a synthetic form is available as nabilone.<sup>1</sup> These drugs are used medically in people to combat nausea caused by chemotherapy and to decrease intraocular pressures caused by glaucoma.<sup>1</sup> They are also used as appetite stimulants in patients with anorexia secondary to AIDS.<sup>2</sup> Common street names for marijuana include pot, Mary Jane, weed, THC, grass, and ganja.<sup>1</sup> The concentration of THC in marijuana varies from 1% to 8%. In hashish, which is derived from the resin of the flowering tops of the hemp plant, the concentration varies from 3% to 6%; in hash oil it varies from 30% to 50%.<sup>1</sup>



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## Clinical signs

Animals usually are exposed to marijuana by accidentally ingesting it. Since January 1998, veterinarians at the ASPCA Animal Poison Control Center (APCC) have consulted on more than 250 such cases. Dogs account for 96% of the exposures, cats account for 3%, and other species account for 1%. According to the ASPCA APCC Database, the most common side effects of marijuana toxicosis are depression, ataxia, and bradycardia. Other signs include agitation, vocalization, vomiting,

diarrhea, hypersalivation, tachycardia, hypothermia, mydriasis, urinary incontinence, seizures, and coma.

In one case reported to the ASPCA APCC, a 29.7-lb (13.5-kg) dog that ingested 3 g marijuana exhibited ataxia, head bobbing, and vocalization. In another case, a 37.4-lb (17-kg) dog that ingested 1 tsp marijuana exhibited bradycardia and ataxia. In both cases, clinical signs occurred within two hours of ingestion.

## Mechanism of action

Marijuana smoke contains up to 61 different cannabinoids.<sup>3</sup> THC is the predominant psychoactive agent of marijuana.<sup>3</sup> THC acts on a unique receptor in the brain that is selective for cannabinoids.<sup>4</sup> This receptor is primarily responsible for the central nervous system effects of cannabinoids.<sup>4</sup> Cannabinoids interact with many neurotransmitters and neuromodulators, including acetylcholine, dopamine,  $\gamma$ -aminobutyric acid, histamine, 5-hydroxytryptamine, norepinephrine, opioid peptides, and prostaglandins.<sup>4</sup> Cannabinoids stimulate dopamine release; enhance  $\gamma$ -aminobutyric acid turnover; and may enhance norepinephrine, dopamine, and 5-hydroxytryptamine formation.<sup>4</sup>

## Pharmacokinetics

In people, plasma concentrations of THC peak five to 12 minutes after inhalation and two to three hours after ingestion.<sup>1</sup> The onset of effects occurs within six to 12 minutes after inhalation and 30 to 60 minutes after ingestion.<sup>1</sup> The most common route of exposure for animals is oral. In dogs, the onset of action occurs 30 to 90 minutes after ingestion, and signs may last up to 72 hours (ASPCA APCC Database: Unpublished data, 2002).

In people, cannabinoids are lipid-soluble; 97% to 99% protein-bound; and partition into many areas of the body, including the heart, fat, salivary glands, liver,

"Toxicology Brief" was contributed by Caroline W. Donaldson, DVM, ASPCA Animal Poison Control Center, 1717 S. Philo Road, Suite 36, Urbana, IL 61802; (888) 4ANI-HELP. The department editor is Petra A. Volmer, DVM, MS, DABVT, College of Veterinary Medicine, University of Illinois, Urbana, IL 61802. Dr. Volmer is also a diplomate of the American Board of Toxicology.

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brain, and kidneys.<sup>1</sup> After ingestion, THC has a substantial first-pass effect.<sup>1</sup> It is metabolized by liver microsomal hydroxylation and nonmicrosomal oxidation.<sup>1</sup> The main route of excretion is through the bile.<sup>1</sup> Within 72 hours of ingestion, about 35% of an oral dose is excreted in the feces as unconjugated metabolites, 10% to 15% is excreted in urine as acidic metabolites and conjugates, and a small portion is excreted

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unchanged in urine.<sup>1</sup> THC's plasma half-life is short because of lipid solubility, but its biologic half-life is long (*i.e.* 25 to 30 hours) because of adipose storage.<sup>1</sup> By five days after exposure, 80% to 90% of the marijuana has been eliminated.<sup>1</sup>

### Toxicity

An LD<sub>50</sub> has not been established in dogs or cats. Research in dogs and monkeys showed that oral doses of delta 9-THC and delta 8-THC ranging from 3,000 to 9,000 mg/kg were not lethal, and all dogs recovered within 24 hours of ingestion.<sup>5</sup> At higher doses, clinical signs in monkeys persisted up to five days.<sup>5</sup> No histopathologic lesions have been noted in dogs or monkeys.<sup>5</sup> After ingesting 3,600 mg/kg of delta 9-THC, rats developed mild to moderate lesions, including splenic hypocellularity, lung congestion, pneumonitis, thymic congestion and hemorrhage, and adrenal congestion.<sup>5</sup>

### Diagnosis

If an animal presents with an acute onset of ataxia, depression, or recumbency, consider marijuana toxicosis as a differential diagnosis. Other differential diagnoses include oral or other exposure to ethanol, ethylene glycol, ivermectin, opioids, barbiturates, benzodiazepines, and phenothiazines. In some cases of marijuana

exposure, signs can improve when the animal is stimulated, or the animal may appear hyperesthetic briefly before returning to the previous clinical presentation. Bradycardia, mydriasis, and urinary incontinence are also often noted.

No specific serum chemistry profile abnormalities are expected with marijuana intoxication.<sup>1</sup> Marijuana may precipitate seizures in people with preexisting seizure disorders, but it is unknown whether this occurs in animals.<sup>1</sup> Urine drug testing can help confirm exposure, but the amount of drug ingested, time elapsed since ingestion, and water consumption after ingestion may affect the results.<sup>1</sup> Increased water consumption may elicit a false negative result.<sup>6</sup>

Obtaining an accurate history can be difficult in cases of illicit drug exposures. Direct, nonthreatening questioning is the best means to try to obtain a correct history. Consult your local and state regulations regarding whether you should report cases of marijuana exposure to the authorities.

### Treatment

Treating marijuana toxicosis involves minimizing absorption and initiating symptomatic and supportive therapy. Induce emesis within 30 minutes only in asymptomatic animals. Administering activated charcoal every eight hours for the first 24 hours helps reduce the severity and duration of signs resulting from enterohepatic recirculation.<sup>7</sup> If the animal is recumbent, use charcoal cautiously because of the risk of aspiration. Monitor respiratory function (since secondary aspiration pneumonia from prolonged recumbency can occur), cardiac function, and body temperature.

For symptomatic animals, supportive care includes intravenous fluid administration (lactated Ringer's or saline solution starting at maintenance rate), thermoregulation, and alternating the animal's body position every four hours. Diazepam is preferred for agitated patients requiring sedation. Use a low dose initially (0.25 to 0.5 mg/kg intravenously) in dogs to prevent excessive sedation.

### Prognosis

Out of more than 250 cases of accidental marijuana ingestion reported to the ASPCA APCC, two deaths were reported. In one cat, exposure to multiple agents was possible, and the results of a gross necropsy revealed that the animal probably died of complications of cardiomyopathy. The second death reported was a horse with signs attributed to colic, but a gross necropsy was not done. The prognosis is favorable for symptomatic animals with no secondary complications, such as aspiration pneumonia. With supportive care, these animals usually recover within 72 hours.

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