



Evaluation of trends in marijuana toxicosis in dogs living in a state with legalized medical marijuana: 125 dogs (2005–2010)

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Abstract

Objective – To report a correlation between the increased number of medical marijuana licenses and marijuana toxicosis in dogs in a state with legalized marijuana for medical use.

Design – Retrospective case series from January 1, 2005 to October 1, 2010.

Setting – Private specialty referral hospital and a university teaching hospital.

Animals – A total of 125 client-owned dogs presenting for known or suspected marijuana toxicosis with or without a urine drug screening test (UDST).

Interventions – None.

Measurements and Main Results – During the study period, 125 dogs were evaluated including 76 dogs with known marijuana exposure or a positive UDST (group 1), 6 dogs with known marijuana ingestion and a negative UDST (group 2), and 43 dogs with known marijuana ingestion that were not tested (group 3). The incidence of marijuana toxicosis presenting to both hospitals increased 4-fold, while the number of people registered for medical marijuana in the state increased 146-fold in the last 5 years. A significant positive correlation was detected between the increase in known/suspected marijuana toxicosis in dogs (groups 1–3) and the increased number of medical marijuana licenses (correlation *R* coefficient = 0.959, *P* = 0.002). Two dogs that ingested butter made with medical grade marijuana in baked products died.

Conclusions – A significant correlation was found between the number of medical marijuana licenses and marijuana toxicosis cases seen in 2 veterinary hospitals in Colorado. Ingestion of baked goods made with medical grade tetrahydrocannabinol butter resulted in 2 deaths. UDST may be unreliable for the detection of marijuana toxicosis in dogs.

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Keywords: canine, illicit drug, intoxication, THC

Abbreviations

CSU	Colorado State University
THC	tetrahydrocannabinol
UDST	urine drug screening test
WRVS	Wheat Ridge Veterinary Specialists

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The authors declare no conflict of interests.

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Introduction

Marijuana is a commonly used recreational and medicinal drug. The dry leaves and flowers from the hemp plant *Cannabis sativa* contain the toxic compound of Δ^9 -tetrahydrocannabinol (THC).¹ Toxicosis in dogs can be caused by inhalation of the smoke, direct ingestion of the leaves, seeds, stems and flowers of the plant, ingestion of products laced with marijuana leaves, or ingestion of products made with concentrated THC or hashish oil.² Clinical signs may be seen within 30–60 minutes after ingestion of marijuana.³ THC toxicosis in dogs can cause considerable morbidity. The most common reported clinical signs of marijuana toxicosis in dogs include CNS depression, ataxia, mydriasis, increased sensitivity to motion or sound, hyperesthesia, ptialism, tremors, and the acute onset of urinary incontinence.^{4,5}

In the 2000 general elections, the people of Colorado passed Amendment 20 that legalized the sale of

marijuana for medical use. In June 2001, the public was permitted to start applying for registry identification cards. By September 30, 2010, there were more than 106,000 registered medical marijuana users in the state of Colorado.⁶ In August 2010, there were 717 licenses issued to medical marijuana dispensaries in the state.⁷

The diagnosis of marijuana exposure may be supported with a urine drug screening test (UDST);^a however, this kit has not been validated for use in dogs. At this time, there is no valid test for detecting THC in canine patients. THC is highly lipophilic and is quickly converted in the lungs and liver to 11-OH- Δ^9 -THC.⁸ In addition to 11-OH- Δ^9 -THC, dogs also metabolize THC to 8-OH- Δ^9 -THC with additional β -oxidation.⁹ Additional conjugated THC metabolites in dogs may cause false negative UDST results due to failure of the human UDST to detect the unique canine THC metabolites.¹⁰

Since the legalization of medical marijuana in Colorado, the authors have subjectively observed an increased frequency in THC toxicosis in dogs. We hypothesized that as the number of medical marijuana licenses increased, so would the number of THC toxicosis cases in dogs. The purpose of this study was to determine if there was a correlation between the increasing number of medical marijuana licenses and marijuana toxicity in dogs presenting to 2 hospitals in a state with legalized medical marijuana. In addition, we aimed to report on the utility of a UDST to diagnosis marijuana ingestion in dogs, as well as to report the death of 2 dogs associated with ingestion of marijuana butter.

Materials and Methods

A retrospective review of medical records at Wheat Ridge Veterinary Specialists (WRVS) and at the College of Veterinary Medicine, Colorado State University (CSU) was performed. Medical records were searched from January 1, 2005 through October 1, 2010 for charts coded with a known or suspected diagnosis of marijuana toxicosis, and all dogs coded with toxicity as a diagnosis. A total of 179 cases of known or suspected marijuana toxicity were found and those medical records were reviewed. Inclusion criteria included dogs that presented between the study dates with complete medical records and where the diagnosis of marijuana exposure was confirmed by UDST, or by witnessed ingestion admitted by the owner. A total of 125 dogs met the inclusion criteria, and the data from both hospitals were combined for statistical analysis.

THC urine testing using a UDST was performed at the clinician and owner's discretion at the time of presentation. Results of the UDST were interpreted by the primary clinician on the case. Positive results were reported when the test line was absent and the control

was present, as well as when the test line was deemed to be significantly fainter than the other tests and the THC control line, and when reported as a positive by the primary clinician in the chart.

Dogs were assigned into 1 of 3 groups based on known or suspected marijuana ingestion. Dogs were considered to be a known ingestion if the owners stated that the dogs were witnessed ingesting marijuana or marijuana-containing products, or there was evidence in the house of marijuana ingestion by the dogs when the owners returned home. Group 1 included dogs with a positive UDST, and known marijuana ingestion, known exposure in their environment, and highly suspected by the clinician or owner. Group 2 included dogs with a negative UDST and known marijuana ingestion. Group 3 included dogs that were not tested with a UDST, but had a known marijuana ingestion.

Data recorded from the medical records included presentation date, signalment, weight, current medications, time of exposure to presentation if known, ingestion of other known toxins, known or suspected ingestion of marijuana, neurologic signs, urinary incontinence, hyperesthesia, pupil size, vomiting prior to presentation, results of UDST, or other presenting complaints. In addition, characteristics of hospitalization such as the performance of a complete physical exam, if the dog was hospitalized for treatment, the duration of hospitalization, any treatments performed (including induction of emesis, administration of activated charcoal, or intravenous fluids), disposition at discharge, and follow-up if available were recorded.

Statistical Analysis

Analyses were performed using commercial statistical software.^{b,c} Kruskal-Wallis one-way analysis of variance on ranks was used to determine statistical medians and differences for age, weight, temperature, pulse, respiratory rate, time from exposure to presentation, and time of hospitalization. Percentages are reported for number of dogs with ataxia, tremors/shaking/twitching, mentally dull/obtunded/disoriented, hyperesthesia, pupil size, vomiting prior to presentation, ingestion with chocolate, and if the patient was alive at discharge. Correlations were performed by calculating a Pearson product-moment correlation coefficient and its associated *P* value. A *P* value < 0.05 was considered statistically significant. Where possible, the correlation coefficient (*r*) was reported as a value between -1.0 and 1.0. A simple linear regression model was used for regression and an adjusted *R*² value (coefficient of determination) was reported as an estimator of how well future outcomes could be predicted by the model.

Results

Marijuana toxicosis statistics in dogs – Study population consisted of 125 dogs, 63 males (19 sexually intact and 44 castrated), and 62 females (16 sexually intact and 46 spayed). Breeds included Labrador Retrievers (13), Golden Retrievers (7), Chihuahuas (6), Terriers (6), Pit Bull Terriers (5), German Shepherd Dogs (4), Boxers (4), Border Collies (3), Pomeranians (2), Rottweilers (2), Bichons (2), Schnauzers (2), Rat Terriers (2), Bull Dogs (2), Pugs (2), Staffordshire Terrier (2), Dachshunds (2), and mix breed dogs (22). The remaining 37 dogs were each single representatives of various other pure breeds.

The most common clinical signs in all groups included ataxia (88%), mentally dull/obtunded/disoriented (53%), mydriatic pupils (48%), urinary incontinence (47%), hyperesthesia (47%), tremors, shaking, or twitching (30%), and vomiting (27%). Combined marijuana and chocolate toxicity occurred in 21% of dogs. Over half (58%) of the dogs were treated as outpatients. In groups 1 and 2, there was 100% survival to discharge, and in group 3, a 95% (41/43) survival to discharge. Three dogs were given an intralipid^d bolus (2 mL/kg, IV) followed by a continuous rate infusion at 4 mL/kg, IV. There was no significant difference in age, weight, heart rate, respiratory rate, temperature, time to presentation, or duration of hospitalization between groups.

In groups 1 and 2, the total number of marijuana toxicosis cases increased 4.4-fold from 2005–2010 with a correlation coefficient of 0.933 ($P = 0.007$) when compared to the rise in medical marijuana registry card holders. In group 3, the total number of marijuana toxicosis cases increased 3.25-fold from 2005–2010 with a correlation coefficient of 0.95 ($P = 0.004$) when compared to the rise in medical marijuana registry card holders. When groups 1–3 are combined, the total number of marijuana toxicosis cases increased 4-fold from 2005–2010, with a correlation coefficient 0.959 ($P = 0.002$) to medical marijuana registered card holders. A summary of marijuana toxicity cases and the number of medical marijuana registry cards by year is summarized in Figure 1.

The total number of emergencies seen at WRVS averaged 5,766 a year (range 5,389 [in 2009] to 6,430 [in 2007]). The number of THC toxicosis cases in all groups at WRVS increased from 1.5 cases per 1000 visits in 2005 to 4.5 THC toxicosis cases per 1000 visits in 2010. The average number of cases seen at CSU in all small animal departments averaged 21,527 a year (range 19,200 [in 2005] to 24,824 [in 2010]). The number of THC toxicosis cases in all groups at CSU increased from 0.16 cases per 1000 visits in 2005 to 0.81 THC toxicosis cases per 1000 visits (2010).

Marijuana toxicity deaths

Two dogs, a 9-year-old male castrated Schipperke and a 7-year-old spayed female Cocker Spaniel, died during treatment after ingesting baked goods made with THC butter. Dog 1 ingested approximately 6 chocolate chip cookies made with medical grade marijuana butter and was found comatose by his owner. Approximately 40 hours after ingestion of THC cookies, the dog died in the hospital. Dog 2 ingested an 8-inch square pan of brownies made with butter into which medical grade marijuana THC had been extracted and 3 kinds of unknown chocolate, and presented comatose to the hospital. Dog 2 went into cardiac and respiratory arrest 10 hours after presentation and 14 hours after ingestion of the brownies.

Medical marijuana registry statistics

In 2005, 730 Coloradoans were registered for medical marijuana identification cards. Medical marijuana registry cards increased logarithmically each year and by September 30, 2010, there were 106,653 active and valid marijuana registry cards, which is a 146-fold increase in 5 years.⁶

Discussion

Results from our study support the hypothesis that as the number of medical marijuana licenses increased, so did the number of THC toxicosis cases in dogs presenting to our hospitals. However, it is possible that the clinicians' index of suspicion for THC toxicosis has increased throughout the years because of the change in legal status of marijuana in Colorado. Moreover, THC toxicity may have been underdiagnosed in the past, prior to the change in legal status of marijuana.

The increased number of THC-intoxicated dogs presenting to our hospitals in all 3 groups appears to be strongly correlated with the increasing number of medical marijuana licenses being issued. Although correlation is suggestive, it does not imply causality. It is possible that the increased number of THC dogs presenting to our hospitals are due to other factors such as increased clinician awareness, population changes, or an increased willingness of clients to seek medical attention for their dogs.

The number of THC toxicosis cases was controlled for the number of cases presenting to the hospitals, and the number of UDST used in the hospital. The average number of UDST utilized for toxicity cases presenting at WRVS averaged 28 (range 23–35) tests per year over the 5 years. Therefore, the increased incidence in THC dogs presenting over the last 5 years is unlikely to be a result of increased testing within the hospital. The number of

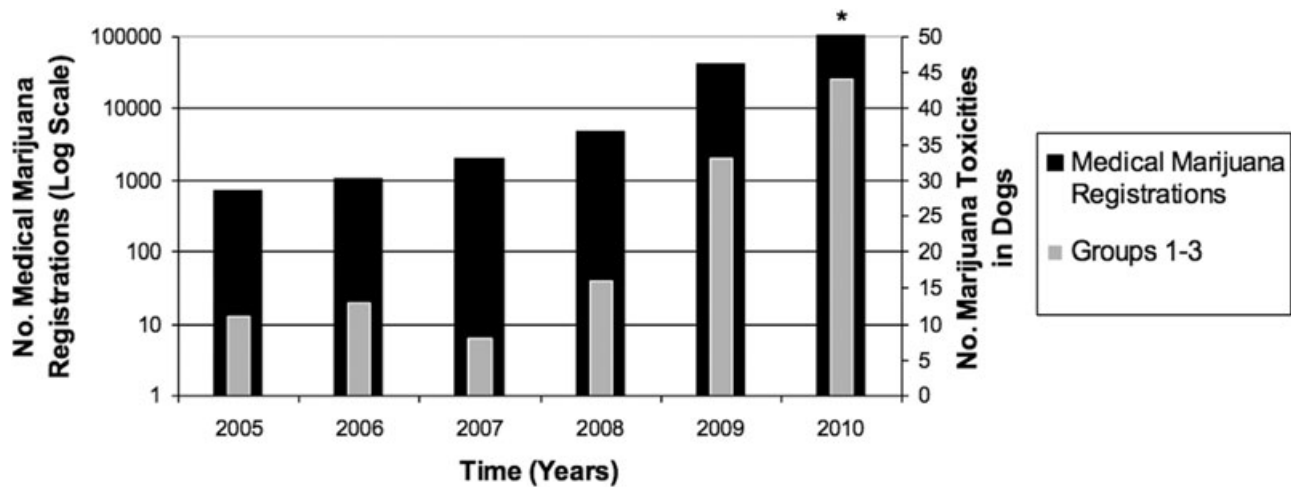


Figure 1: Total number of medical marijuana registry cards and all dogs with THC toxicosis. *The number of registered users as of September 30, 2010 and is not the complete year.

THC toxicosis cases was not controlled for the increased population in the state of Colorado from 2000 (4.3 million people) to 2010 (5 million people).^{11,12} It is possible that the increased number of people living in Colorado contributed to the increased number of medical marijuana card holders or the number of THC toxicosis cases; however, the increased population did not result in an increased number of hospital visits and therefore is unlikely to be the cause of the increased THC toxicosis cases evaluated.

In the present study, ataxia and depression were the most common clinical findings at presentation for dogs with THC toxicosis that are similar to previous reports.¹³ However, the number of dogs with urinary incontinence (47% versus 5%), hyperesthesia (47% versus 6%), and mydriasis (48% versus 11%) were markedly higher in the present study.¹³ The difference in the clinical signs reported in the present study compared to the previous veterinary report may be attributed to differences in data collection between the studies. While the previously published study was an American Society for the Prevention and Cruelty of Animals (ASPCA) Animal Poison Control Center database review, this study evaluated symptomatic patients presented to a veterinary hospital. Poison control center data may also reflect a population of animals that are only exposed to THC, but asymptomatic (ie, the owner phoned for advice, rather than presenting the animal to a veterinarian). The poison control center case review may also be limited to the information given initially over the phone by the client or the veterinarian. It is not clear in the previous study how many American Society for the Prevention and Cruelty of Animals documented exposures went on to seek medical attention.

Almost half of all dogs in this study presented with urinary incontinence, which is much higher than previously reported.¹³ It is possible that dogs that are exposed to medical grade marijuana have a higher incidence of urinary incontinence. The additional THC metabolite 8-OH- Δ^9 -THC produced by dogs may explain why urinary incontinence is seen in dogs and not in other species, however, further studies are needed to evaluate the cause of urinary incontinence with THC toxicosis.

The second purpose of this study was to report on the use of an UDST for THC detection in dogs based on known THC ingestion. Group 2 included six dogs with known THC ingestion as reported by the owners and a negative UDST. The UDST is a 5-channel urine dip stick with a colorimetric bar and control that is designed for humans to test for illicit drugs. The UDST utilizes a dye immunoassay across a permeable membrane. When the drug metabolite is present, it binds to the drug/protein conjugate at the test line and does not allow the dye conjugate to bind.¹⁰ The limit of detection of the THC channel is 50 ng/mL. False negatives (Group 2) may be seen with testing too recently after exposure. In addition to 11-OH- Δ^9 -THC, dogs also metabolize THC to 8-OH- Δ^9 -THC with additional β -oxidation.⁹ This altered metabolite may contribute false negatives when using the human UDST.¹⁰ Samples being tested for THC must also be handled appropriately, because THC can bind to rubber stoppers and glass and give false negative results.

The human UDST has not been validated for use in dogs and its usefulness remains controversial. The findings in this report suggest that the UDST may be unreliable and only be helpful if the test is positive. In one report, the UDST was shown to not detect the presence of THC in dogs with known marijuana ingestion. In

the same report, THC was also not detectable using gas chromatography/mass spectrometry.¹⁰ Two other dogs were reported to have variable positive test results using liquid chromatography/mass spectrometry and ELISA testing. The UDST used by both hospitals in this report is of a different manufacture than the reported UDST used in the published report¹⁰ and differences may exist in specificity and sensitivity.

The UDST directions for interpretation of results of human urine indicate that no binding of dye in the test site and dye binding at the control site is to be interpreted as a positive. At this time, there is no scientific laboratory test (ELISA, gas chromatography, liquid chromatography, mass spectrometry) that reliably detects THC in the urine of dog and, therefore, interpretation of the UDST must be used with caution. Lateral flow colorimetric assay tests utilize the concept of a bound protein or antibody receptors at the test line that capture the antigen/antibody or drug. The capturing of the substance in question covers the binding sites for the control substance bound with the dye that enables the visual interpretation of the test. Many lateral flow assays, along with the control site to ensure the test was run properly, employ a "weak positive" and a "strong positive" site of binding. Therefore, it may reasonable to interpret a test line with a fainter binding of dye than the control line as a weak positive because the receptors are being occupied by the test substance. Until a laboratory test is developed that can detect THC in dog urine, no cage-side tests can be validated and all cage-side tests for the detection of THC should be used with caution.

The third purpose of this study was to report on 2 dogs that died after ingesting THC butter with an unknown concentration of THC. Dog 1 was obtunded at presentation and only minimally responsive to painful stimuli. Decontamination measures were recommended; however, the patient was not deemed alert enough to administer oral activated charcoal,^e and the owners declined orogastric lavage. Based on the severity of clinical signs, intralipid therapy was offered to the owners. An intralipid^d bolus (2 mL/kg, IV) was administered followed by a continuous rate infusion (4.1 mL/kg/h, IV) for 19 hours. Approximately 38 hours after presentation, the patient developed a coagulopathy characterized by bruising on the abdomen, hematemesis, and epistaxis, followed by respiratory and cardiac arrest. The coagulopathy was not further classified prior to the dog's death.

Dog 2 was hospitalized and decontamination measures included orogastric lavage and orogastric administration of activated charcoal. Intralipid therapy was declined by the owners. During the course of hospitalization, the patient remained comatose and developed hypoxia (SpO₂ 80% with flow-by oxygen, 2 L/min)

and began panting. Mechanical ventilation was recommended and the owners declined. The patient went into cardiac and respiratory arrest 10 hours after presentation and 14 hours after ingesting brownies made with medical grade marijuana butter.

In a previous 2004 report of marijuana toxicosis in 213 dogs, there were no case fatalities.¹³ In this report of 125 dogs, some with exposure to medical grade marijuana, there were 2 deaths in dogs that were exposed to medical grade marijuana butter in baked goods. THC butter is made by boiling parts of the hemp plant to extract the lipophilic THC. Butter is then added to allow the THC to infuse into the butter. Lethal toxicity is reportedly rare with the THC LD₅₀ = 3000 mg/kg in dogs.^{2,13} Both dogs that died in this study likely ingested significantly lower doses than the LD₅₀ of THC; however, it is also possible that these dogs were more sensitive to THC or THC butter contains additional compounds that can be fatal in dogs. In addition, medical grade THC butter may have a higher concentration of THC or is metabolized differently in dogs. Dogs that are exposed to THC butter and THC butter containing products may benefit from earlier, more aggressive treatments.

Both dogs that died ingested THC butter and chocolate. However, 26 other dogs also ingested a combination of chocolate and marijuana and survived. Both dogs had clinical signs that can be attributed to chocolate ingestion such as hypo/hypertension and bradycardia/tachycardia; however, neither dog developed ECG changes, hyperactivity, or seizure-like activity. Although it is possible for dog 2 to have ingested a lethal dose of chocolate, it seems unlikely to be the sole cause of death. In addition, both dogs vomited while presumably unable to fully protect their airways due to their mentally dull states. Dog 1 did not develop respiratory signs prior to arrest; however, he had evidence of other foreign material in his vomit that may have contributed to his presumably septic state and death. Dog 2 began panting and became hypoxic prior to arrest; however, the owners declined chest radiographs and mechanical ventilation, and aspiration pneumonia cannot be ruled out in this dog. The cause of death in both of these dogs cannot be definitely linked to the THC ingestion, but presumably it was a significant contributing factor.

The percentage of THC in each batch of marijuana, and within the plant itself, can be variable. The University of Mississippi Potency Monitoring Project has reported a more than doubling in THC content in marijuana seized by law enforcement officers over the last 25 years.¹⁴ It is possible that the number of THC toxicosis cases has not increased, but because of more potent forms of marijuana, including medical marijuana, the clinical signs are worse, prompting more owners to seek medical attention

or, because of worse clinical signs, more cases are diagnosed. In addition, dogs that are exposed to more potent marijuana may require more aggressive decontamination measures and treatments.

The use of intralipid therapy in dogs for marijuana toxicity has not been previously reported to the authors' knowledge. THC is a very highly lipophilic drug and the use of lipid may be effective in treating cases of toxicity involving other lipophilic compounds such as THC and reduced clinical signs. Lipid therapy has been shown to be effective in other highly lipophilic toxicity cases in both dogs and cats.^{15,16} Three dogs were given intralipid therapy in this report, with 2 dogs surviving. In the 2 surviving dogs, no adverse effects of the intralipid therapy were observed, but further clearance studies need to be performed to assess the efficacy of lipid therapy in dogs for THC toxicosis. In the one dog that died, it is unlikely that lipid therapy contributed significantly to the cause of death.

There are several limitations of this study including the retrospective case review. The number of THC toxicosis cases in dogs is correlated with the increasing number of medical marijuana card holders; however, all external factors such as population growth, socioeconomic status, and Colorado dog population changes cannot be controlled for in this study. In addition, only 1 large specialty hospital and 1 university hospital were used to compile data in this study. It is possible that THC cases are overrepresented in the neighborhoods surrounding these hospitals and are not representative of the whole state.

Over the time frame studied at 2 hospitals, there were many clinicians interpreting the UDST and inconsistencies or human error cannot be ruled out in the interpretation of the UDST; however, all dogs in the study were known or suspected of THC ingestion and regardless of the UDST results. It is possible that a very small number of dogs that experienced signs consistent with THC intoxication were misclassified as suspected THC ingestion dogs with a false positive UDST. Other differentials of THC ingestion may include other prescription/controlled medication including barbiturates, benzodiazepines, opioids, ethylene glycol, and ethanol.¹ Once a validated laboratory test is developed that can detect the canine THC metabolite, a prospective trial evaluating the UDST is warranted.

In addition, there was not enough consistency in the medical records to determine which dogs were exposed to street grade marijuana and which dogs were exposed to medical grade marijuana. Anecdotal observations are that it is now more common to hear from owners that the marijuana their pet was exposed to was of medical grade because they are a registered medical marijuana user; however, those statements may also be untruthful

due to the illegal nature of having marijuana without being a registered user.

There are several limitations in this study in regard to the 2 dog deaths. Both dogs ingested other compounds that are known to cause death in dogs, but the suspected doses were unlikely to be high enough to be fatal. Both dogs were known to have ingested THC butter, but THC concentrations were not tested to determine if the serum THC concentration in the dogs were fatal. In addition, other compounding factors such as the decreased mental state due to the THC ingestion leading to secondary aspiration pneumonia, pancreatitis secondary to the butter or the chocolate, sepsis, and multiorgan failure cannot be ruled out in these dogs. Dog 2 died only 10 hours after ingestion of THC butter, making death secondary to pancreatitis less likely. Although if secondary causes of death were present, the THC butter ingestion was likely still a contributing factor if not the primary process that led to death in these 2 dogs.

Conclusions

This study describes the exponential increase in medical marijuana registry participants in a state that has legalized medical marijuana with a significant increase in marijuana toxicosis cases that have presented to 2 large hospitals including 2 deaths during the last 5 years. As medical marijuana becomes more available to the general population, an increase in the number and severity of marijuana toxicity cases may also be seen in companion animals. Dogs ingesting medical grade marijuana butter products may be at higher risk of serious complications and earlier aggressive treatment may be warranted. In addition, the UDST may be unreliable and its interpretation should be used with caution and further testing is warranted.

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Footnotes

- ^a 5 Panel One Step Drug of Abuse Urine Test, Meditests, Bensalem, PA.
- ^b Microsoft Excel, Microsoft Office XP Professional, Redmond, WA.
- ^c Minitab 16 Statistical Software, version 16.1.1, Minitab Inc., State College, PA.
- ^d Liposyn III, Hospira Inc., Lake Forest, IL.
- ^e NICH UAA Gel, NICH Marketers, Inc., Gulf Breeze, FL.

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