SAVING PETS' LIVES, 24 HOURS A DAY, 7 DAYS A WEEK
PET POISON HELPLINE

Nationwide

A Year in Review: What's New in the Veterinary Toxicology Literature

June 7, 2016

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Veterinary Medical and Surgical Group
Ventura, CA

What is Pet Poison Helpline?

- 24/7 animal poison control center
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    - DACVIM
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Carol McConnell, DVM, MBA
Chief Veterinary Officer
April 2016

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- All preventive care including vaccinations, teeth cleaning and spay/neuter

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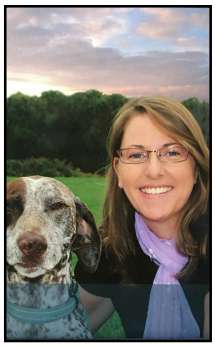
Speaker Introduction



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Outline

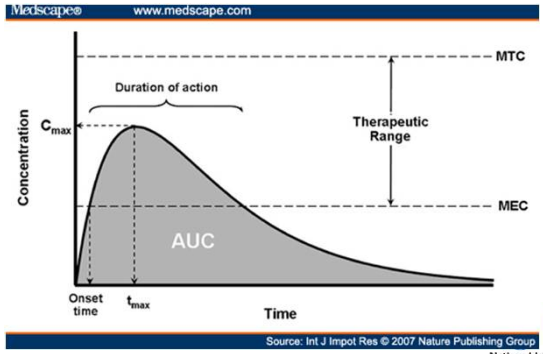
- Literature Review:
  - Carprofen
  - Cocaine
  - Emesis in cats
  - Marijuana
  - Metaldehyde and iron toxicosis
  - Methionine
  - Tea Tree Oil
  - Walnuts (black walnut)
  - Xylitol

Carprofen

- Compare the effectiveness of activated charcoal alone versus the combination of emesis and activated charcoal in preventing carprofen absorption
- 6 dogs, 15mg/kg carprofen
  - At 30 mins: AC administered (2g/kg)
  - At 30 mins: Emesis + AC administered (2g/kg)
  - Control group
- Both AC and emesis + AC significantly reduced AUC and $T_{1/2}$
- AC (NOT emesis+AC) significantly reduced Tmax

1) Schildt J, Jutkowitz LA, Beal MW2, et al. Effect of Activated Charcoal Alone Versus Emesis and Activated Charcoal on Carprofen Absorption Following Experimental Overdose in Dogs. J Vet Emerg Crit Care 2009; 19(s1):A6-A7.

Pharmacokinetics



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Carprofen

- Compare the effectiveness of activated charcoal, activated charcoal + sorbitol, and multi-dose activated charcoal in preventing carprofen absorption
- 8 dogs, 120mg/kg Carprofen + AC, ACS, MD
  - AC, ACS, and MD significantly reduced AUC
  - AC and MD (NOT ACS) significantly reduced Cmax
  - There were no differences in AUC or Cmax among the AC, ACS, and MD groups
  - MD significantly reduced $T_{1/2}$ when compared to the control group.
  - $T_{1/2}$ did not differ significantly among AC, ACS, and the control group
  - Tmax was not affected by any treatment

2) Koenigshof AM, Beal MW, Poppenga RH, et al. Effect of sorbitol, single, and multidose activated charcoal administration on carprofen absorption following experimental overdose in dogs. J Vet Emerg Crit Care. 2015

Nationwide

Cocaine

- Characterize the incidence, signalment, presenting complaint, history, clinical signs, diagnostic test results, complications, treatment, length of hospitalization, and outcome of dogs presenting with presumptive cocaine toxicosis
- 19 dogs with + urine drug screen (March 2004 to March 2012)
- Neurological abnormalities = all dogs
  - Mydriasis (11/19 [58%])
  - Hyperexcitability/hyperesthesia (10/19 [53%])
  - Ataxia (8/19 [42%])
  - Focal or generalized muscle tremors 8/19 [42%])
  - Reduced mental awareness (6/19 [32%])
  - Seizures (3/19 [16%])
- Other signs included weakness (7/19 [37%]), vomiting (6/19 [32%]), and lethargy (3/19 [16%])
- CV signs:
  - Tachycardia (sinus tachycardia) was apparent in (10/19 [53%])
  - Hypertension in (4/19 [21%])
  - Hyperthermia in (5/19 [26%])
- Blood work: hyperglycemiain (4/19 [21%]) dogs and hyperlactatemiain (9/19 [47%])

Thomas EK, Drobatz KJ, Mandell DC. Presumptive cocaine toxicosis in 19 dogs: 2004–2012. JVECCS 2014; 24(2): 201-7

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Cocaine

- Treatment:
  - None (3/19 dogs)
  - 16/19 hospitalized (median 15hrs (range 10-30hrs)
  - All dogs received IVF therapy
  - 9/16 received benzodiazepines (seizure vs sedation)
    - 2/3 refractory to benzodiazepines (Phenobarbitalvs propofol)
  - 4 dogs received acepromazine for sedation when benzodiazepines were ineffective
- Hypertension and tachycardia generally responded to sedatives; one case received esmolol CRI
- Prognosis for survival was good, with supportive care

Emesis Induction in Cats

IM Dexmedetomidine and xylazine comparison

- 47 cats
  - 21 xylazine
  - 26 dexmedetomidine
- 24/47 (51.1%) vomited successfully
  - 9/21 (43%) xyalzine
  - 15/26 (58%) dexmedetomidine
    not significant (p=0.31)

Xylazine

- 10/21 (48%) > 0.44mg/kg
- 11/21 (52%) ≤ 0.44mg/kg
  not significant (P= 0.53)
  - Median dose of xylazine 0.43 mg/kg
  - Range: 0.36 to 0.64mg/kg

Demedetomidine

- 13/26 (50%) >10µg/kg
- 13/26 (50%) ≤ 10µg/kg
  not significant (P= 0.69)
  - Mean ± SD dose of dexmedetomidine administered was 11 ± 3 µ g/kg

1) Willey JL, Julius TM, Claypool SA, et al.Evaluation and comparison ofxylazine hydrochloride and dexmedetomidinehydrochloride for theinduction ofemesis in cats: 47 cases (2007-2013). *JAVMA 2016;* 248(8): 923-8.

Emesis Induction in Cats

- 43 cats
- **H_2O_2**:
  - In 3 (7%) cats, hydrogen peroxide (1.5- 2.0 mL/kg)
  - No emesis
- **Xylazine**:
  - In 25 (58%) cats, median dose 0.44 mg/kg; range 0.4-0.5 mg/kg
- **Dexmedetomidine**:
  - In 16 (37%) cats, median dose 7µg/kg (range 0.96-10µg/kg)
- **Dexmedetomidine**
  - IM in 7 cats (median dose of 7.0 µg/kg (range 7- 10 µg/kg)
  - IV in 8 cats (median dose of 3.5 µg/kg (range 0.96-10µg/kg)

2) Thawley VJ, Drobatz KJ. Assessment of dexmedetomidineand other agents for emesis induction in cats: 43 cases (20092014). *JAVMA 2015;* 247(12): 1415-18.

Emesis Induction in Cats

- 24/43 (56%) cats vomited
  - 11/25 (44%) Xylazine
  - 13/16 (81%) Dexmedetomidine
- Compared with xylazine, dexmedetomidine was significantly more likely to result in emesis (P = 0.018)
- **Emesis was successfully induced in 7 of 7 (100%) with IM dexmedetomidine and in 6 of 9 (67%) with IV dexmedetomidine**
- IM vs IV efficacy was **not** significantly different (P=0.212)

Marijuana

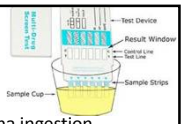
- Retrospective case series:
  - Jan 1, 2005 to Oct 1, 2010
- 125 dogs: known or suspected marijuana exposure
- Purpose of the study:
  - Determine if there was a correlation between the increasing number of medical marijuana licenses and marijuana toxicity in dogs
  - Also to report on the utility of a UDST to diagnose marijuana ingestion in dogs

Meola SD, Tearney CC, Haas SA, et al. Evaluation of trends in marijuanatoxicosis in dogs living in a state with legalizedmedical marijuana: 125 dogs (2005-2010) *J Vet Emerg Crit Care* 2012; 22(6): 690-696)

Marijuana

- Clinical signs:
  - Ataxia (88%)
  - Mentally dull/obtunded/disoriented (53%)
  - Mydriatic pupils (48%)
  - Urinary incontinence (47%)
  - Hyperesthesia (47%)
  - Tremors, shaking, or twitching (30%)
  - Vomiting (27%)
- Combined marijuana and chocolate toxicity occurred in 21% of dogs
- Over half (58%) of the dogs were treated as outpatients
- 2 dogs died

Marijuana



- Group 1: positive UDST, and known marijuana ingestion, known exposure in their environment, and highly suspected by the clinician or owner
- Group 2: negative UDST and known marijuana ingestion
- Group 3: not tested with a UDST, but had a known marijuana ingestion

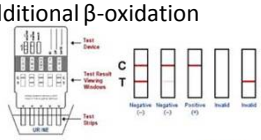
- Groups 1–3 combined: total number of marijuana toxicosis cases increased 4-fold from 2005 to 2010 [correlation coefficient 0.959 (P = 0.002)] when compared to the rise in medical marijuana registered card holders.

Nationwide

Marijuana

- **Why?** Six dogs (known THC ingestion) and a negative UDST…
- The limit of detection of the THC is 50 ng/mL
- False negatives 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

This may contribute false negatives when using the human UDST



Nationwide

Metaldehyde and Iron phosphate

- A pesticide incident database from the NPIC was searched between October 1, 2000, and September 30, 2011
- 50 Metaldehyde products and 28 Iron phosphate products registered by EPA
- Purpose of the study: Report metaldehyde and iron phosphate exposures in animals, characterize iron phosphate exposure incidents in dogs for which signs compatible with iron toxicosis
- Decreased incidence in metaldehyde since 2006
- 1,500 reported exposures to molluscicides containing metaldehyde (n =1,285) or iron phosphate (n = 215)
- 35 deaths associated with metaldehyde, none with iron phosphate

Buhl KJ, Berman FW, Stone, DL. Reports of metaldehyde and iron phosphate exposures in animals and characterization of suspected iron toxicosis in dogs. J Am Vet Med Assoc 2013(242); 1244-8

Iron Toxicosis

- MOA: Iron intake → GI epithelium absorption → bound to ferritin → in the circulation it is carried on transferrin; when these iron binding proteins are saturated → TOXICOSIS
- Iron excretion - GI tract via epithelial cell sloughing OR blood loss
- Iron → free radicals → tissue damage (GI, vascular, liver, heart)

- Clinical signs:
- STAGE 1: (0–6hrs) Damage to the gastric mucosa, depression, abdominal pain, vomiting and diarrhea (+/- blood)
- STAGE 2: (6–24hrs) Apparent recovery
- STAGE 3: (12–96hrs) GI signs return, weakness, shock, GI hemorrhage, tachycardia, cardiovascular collapse, coagulation disorders, and possibly death
- STAGE 4: (2–6wks) Repair of GI injury → fibrosis (not as commonly as stages 1–3)

Metaldehyde and Iron Phosphate

- Subset evaluation: 56 reports involving 61 dogs with suspected iron toxicosis
  - 31/56 (55%) reports involving 34 dogs- exposure occurred after the molluscicide product was applied to a surface
  - 11 (20%) reports involving 12 dogs– exposure to stored product

- Vomiting: most common clinical sign (40/56 [71%] reports involving 43 dogs)
- Diarrhea (24/56 [43%] and hemochezia (n=4)
- Lethargy (14/56 [25%] reports involving 15 dogs)
- Combinations (of above signs) in 21 (38%) reports involving 21 dogs

Methionine

- Descriptive study: Signalment, clinical findings, onset of signs, outcome, and prognosis
- Retrospective: January 2001 to December 2012
- 1,197 calls: 1,525 animals with potential methionine intoxication

- Dosage ranged from 3.9 to 23,462 mg/kg
- Sources: Lawn saver products
  - Other sources (not included in this study) multivitamins, joint care supplements & SAMe
- Females (55%), males (44%)

Hickey MA, Son TT, Wismer T. Retrospective evaluation of methionine intoxication associated with urinary acidifying products in dogs: 1,525 cases (2001–2012). J Vet Emerg Crit Care, 2015

Methionine

- Vomiting: occurred mean 2.8hrs (5mins - 9hrs)
- Ataxia: occurred mean 6.8hrs (1hr -18hrs)

- Resolution of signs (92%) w/in 18hrs – 24hrs, all by 48hrs
- 33% each: at home care, outpatient DVM, hospitalized DVM care
- No fatalities

- Treatment
  - Decontamination (emesis w/in 2-4hrs)
  - IVF therapy, GI supportive therapy, safe housing
  - Correction of electrolyte and acid/base abnormalities

Methionine

Sign	#affected dogs	% affected dogs
Vomiting	623	31.6
Ataxia	386	19.6
Lethargy	94	4.8
Diarrhea	63	3.2
Abnormal posture	53	2.7
Weakness	46	2.4
Polydipsia	40	2.0
Disorientation	28	1.4
Hypermetria	20	1.0
Vocalization	20	1.0
Tremors	20	1.0
Anorexia	20	1.0

Lowest dose 22.5mg/kg

Lowest dose 94.6mg/kg

>300mg/kg

Acidosis (9 cases), hypokalemia (8 cases), and hyperglycemia (7cases)

Tea Tree Oil

- Retrospective study: Review of toxicosis from the use of 100% TTO in dogs and cats, focusing on clinical signs (onset time, types, frequency, duration, and severity) epidemiological information, and treatment
- Australian tree tea oil or melaleuca oil: Obtained by steam distillation of the freshly harvested leaves of *Melaleuca alternifolia* tree leaves
  - Rapidly absorbed orally or via skin due to lipophilic nature
  - >100 components, terpenes predominate (50-60%)
  - Marketed as a antiseptic, fungicide, and skin care agent
- 337 dogs / 106 cats, Jan 2002 to Jan 2012
- Major 31 (7%), moderate 248 (50%), mild 161 (36%)
- Intentionally applied 89%, accidental exposure 2%, unknown 9%
  - Cutaneous (50%), cutaneous & oral (30%), oral (15%), aural (3.6%), IV (1%)

Khan SA, McLean MK, Slater MR. Concentrated tea tree oil toxicosis in dogs and cats: 443 cases (2002-2012). J Am Vet Med Assoc. 2015(244):95-9.

Tea Tree Oil

Dogs

- Major 18 (5%) M
- Moderate 215 (64%)
- Mild 102 (30%)
  - 2 dogs died
- Clinical signs:
  - Lethargy 181 (43%)
  - Paresis/hind limb weakness 150 (45%)
  - Ataxia 144 (43%)
  - Tremors 34 (10%)
  - Vomiting 20 (6%)
  - Coma 15 (5%)
  - Skin 3 (4%)
  - Increased liver enzymes (2%)

Cats

- AGE AND WEIGHT ASSOCIATED WITH SEVERITY
- Major 13 (12%)
- Moderate33 (31%)
- Mild 59 (56%)
  - No deaths reported
- Clinical Signs:
  - Drooling 47 (44%)
  - Ataxia 24 (23%)
  - Lethargy 21 (20%)
  - Coma 17 (16%)
  - Tremors 10 (9%)
  - Hypothermia 8 (8%)
  - Skin 2 (2%)

Nationwide

Tea Tree Oil

- Treatment:
  - Decontamination: bathing with dish soap, e-collar to prevent grooming (cats), single dose of AC/C
  - **NO EMESIS = concern for terepenes (high viscosity molecule) and aspiration risk
  - General supportive care (heat, positional, respiratory, CV, etc)
  - Tremors = methocarbamol vs diazepam
  - Hepatoprotectants = SAMe, Denamarin, Milk Thistle, etc

Nationwide

Walnut (black walnut tree)

- **Purpose of the study:** Identify clinical signs associated with oral exposure to black walnut tree (Juglans nigra) wood, nuts, or nut hulls in dogs
- Compare clinical syndromes between wood ingestion and walnuts or nut hulls
- 93 dogs, Nov 2001 and Dec 2012
- 28 (30%) dogs: wood (50%) or wood shavings (50%)
- Most commonly reported in January, February, and April (12/28 cases)
- Primarily eastern North America
- Time to onset 0.17-19hrs
- The most commonly reported clinical signs for this group of dogs included lethargy or subdued behavior (14 [50%], generalized or hind limb weakness (13 [46%]), vomiting (13 [46%]), stiffness (8 [29%]), ataxia (7 [25%]), and tremors or fasciculations (7 [25%])
- The duration of clinical signs ranged from 1 to 33.25 hours (mean ± SD, 14.4 ± 2 hrs)
- 20/28 hospitalization: IVF, methocarbamol, anti-emetic

Coleman AE, Merola V. Clinical signs associated with ingestion of black walnut tree (Juglans nigra) wood, nuts, and hulls in dogs 93 cases (2001–2012). *JAVMA, 2016;* 248(2): 195-200.

Nationwide

Walnut (black walnut tree)

- 65/93 (70%) cases: walnuts or hulls
- Commonly in September (n = 11), October (16), and December (8)
- Clinical signs in 40 of 65 (62%) cases
- Time to onset observed (n = 37 dogs) ranged from0.02 to 192 hrs
- Most commonly reportedclinical signs: vomiting (31 of 65 [48%], lethargy/subdued behavior (6 [9%]), diarrhea 5 [8%]) and anorexia (4 [6%])
- 15/65 (23%) developed neurological signs: lethargy, disorientation, tremors or fasciculations, ataxia, seizures, and generalized or hind limb weakness

- 17/65 (26%) dogs in this group were treated at a veterinary hospital
- IV or SC fluid administration (n = 6) andantiemetics (2)

Nationwide

Walnut (black walnut tree)

- Frequency of neurologic or musculoskeletal signs in each group
  - Wood 26/28 [93%]
  - Nuts and hulls 15/65 [23%]
- These signs were significantly (P < 0.001) more common in dogs that ingested wood compared to nuts and hulls
- The relative risk of developing neurologic or musculoskeletal signs after ingestion of black walnut wood in dogs was 4.02 times that for dogs that consumed nuts or nut hulls

Nationwide

Xylitol

- Clinical signs in 39 dogs (20%)
  - 24 did not have clinical signs in hospital
  - 9 were not hospitalized
  - 6 continued to have clinical signs in hospital (4/6 vomiting)
- 153/192 dogs = asymptomatic at presentation, 2 developed CS (vomiting)
- Diarrhea (1), partial seizure (1)
- Dogs that developed clinical signs ingested a significantly (P =0.02) higher *estimated dose of xylitol (0.49 g/kg; range 0.12–2.13 g/kg) than those that were asymptomatic (0.30 g/kg; range 0.03–3.64 g/kg)

Estimated xylitol dose was based off 0.3g/piece or 1 g/piece

Nationwide

Xylitol

Blood glucose information for 192 dogs

	Initial BG (mg/dL)	Duration of ↓ BG	Time to lowest BG	Lowest BG mg/dL
Median	86	0	2hrs	72
Range	15-185	0-27hrs	0-58hrs	15-185
#dogs evaluated	178	138	139	177

Blood glucose information in 30 hypoglycemic dogs (BG <60mg/dL)

	Initial BG (mg/dL)	Duration of ↓ BG	Time to lowest BG	Lowest BG mg/dL
Median	55.5	3.5hrs	0.5hr	54
Range	15-117	1-27hrs	0-30hrs	15-60
# dogs evaluated	30	28	30	30

Nationwide

Xylitol

- A majority of dogs (n = 137, 71.3%) had a serum biochemistry profile performed. The most common biochemical abnormality was an increase above the upper end of the reference interval for ALT and/or tBR (n = 30; 21.9%)
- Most dogs had a mild increase in ALT (200 U/L, n = 12), though 4 dogs had an ALT > 800 U/L
- RECHECK: Six dogs had increased liver values, though all values had decreased from hospitalization and all dogs were clinically normal on recheck

Nationwide

Xylitol

Treatment	#	%
Apomorphine	108	56.3
IVF	84	43.8
AC*	53	27.6
Hepatoprotectants	49	25.5
Dextrose	41	21.3
H2O2	27	14.1
Gastroprotectants	20	10.4
Anti-emetics	9	4.7

Only 8-23% absorption in in-vitro study

* The median duration of hospitalization was 18 hours (n = 122; range 1–70 hours)
* All dogs survived to discharge
* 158 were known to be alive at 28 days

Cope RB. A Screening study of xylitol binding in vitro to activated charcoal. Vet Hum Toxicol. 2004; 46(6); 336-7

Nationwide

When in doubt, call 800-213-6680

- Something you're not familiar or comfortable with
- Odd clinical signs
- Animals with preexisting disease

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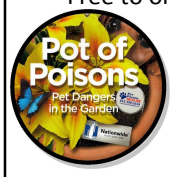

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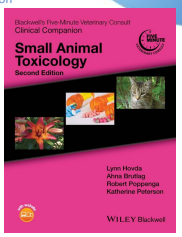

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Hot Topics in Toxicology: Marijuana, Xylitol, and Laundry Pods

APRIL 12, 2016 - Ahna Brutlag, DVM, MS, DABT, DABVT
Let's Chew the Fat: Updates on the Use of Intravenous Lipid Emulsion

JUNE 7, 2016 - Sarah Gray, DVM, DACVECC
A Year in Review: What's New in the Veterinary Toxicology Literature

SEPTEMBER 20, 2016 - Colleen Almgren, DVM, PhD, DABT, DABVT
Vitamins, Minerals, and Herbal Supplements: The Good, the Bad and the Very, Very Bad

NOVEMBER 15, 2016 - Katherine Peterson, DVM, DACVECC
There's No Place Like the Emergency Room for the Holidays: Emergency Care for Holiday Toxins

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Thank you for attending!

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2. **I attended the webinar but wasn't the person who logged in. Can I still get interactive CE credit?** Yes. Send your name and email address to info@petpoisonhelpline.com by 1pm central time on June 8, 2016 (strict deadline).
3. **Can I watch the recorded webinar online for CE credit?** Yes. You can receive non-interactive CE credit. Go to the "For Vets" page on our website, www.petpoisonhelpline.com for more info.

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