Topical Toxins Poisonous to Pets

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Introduction

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Pet Poison Helpline
Minneapolis, Minnesota
VPI® and Pet Poison Helpline® working together

- Shared mission in highlighting the importance of preparing for accidents and poisonings in small animals
- Addressing the cost of veterinary care
  - VPI covers the $39 Pet Poison Helpline fee when a pet is brought in to your hospital for care
- Enabling best medicine
  - Pet owners with VPI Pet Insurance spend twice as much on their pets (single events) than those without VPI Pet Insurance
VPI® and Pet Poison Helpline® working together

- Providing veterinary reviewed pet health information online
  - www.petpoisonhelpline.com/owners
  - www.petinsurance.com/healthzone.aspx

- Providing complimentary pet owner educational materials for your practice - available for ordering:
  - First Aid for Your Pet brochure
  - Poisoning Emergencies brochure
  - Toxins in the Kitchen stickers
  - Toxic Human Meds stickers
  - Emergency Numbers stickers
Pet Poison Helpline

- Animal poison control
  - 24/7 availability
  - $39 one-time fee/case
  - Unlimited case follow-up
  - Access to multiple specialists
    - Board-certified veterinary toxicologists (DABVT, DABT)
    - Emergency/Critical Care (2 DACVECCs, ECC resident)
    - Internal Medicine (DACVIM)
    - Herpetology
    - PharmD/Clinical Pharmacists
How are we different?

• Pet Poison Helpline
  • Staffed by veterinary specialists, veterinarians and veterinary professionals

• SafetyCall International
  • 24/7 human and animal poison control center
  • World’s largest industry poison control
  • Staffed by human medical staff and veterinary professionals

• Call volumes
  – 150,000+ calls/year
  – 65% of calls are animal-related
Topical toxins: Why do we care?

• Seem harmless?

• Natural so, therefore, safe?

• Some tubes are deadly!
Topical toxins

- Zinc oxide
- Corticosteroid creams
- Triple-antibiotic creams
- Pyrethrins
- Tea tree oil

- Fentanyl
- Nicotine
- The DEADLIEST ONES:
  - 5-FU
  - Calcipotriene
Topical Toxins

• Topical “toxin” examples
  – Creams, ointments, essential oils, ocular medications, parasiticides

• Common routes of exposure
  – Topical:
    • Well-meaning owners
    • Labeled products
  – Oral:
    • Accidental ingestions (chewing into the tube)
    • Chronic ingestion of topically applied products
Expected Outcomes

- **Minor**: Mild and self-limiting clinical signs. Little to no treatment needed.
  - Zinc oxide ointments
  - Steroid ointments
  - Antibiotic ointments

- **Moderate**: Systemic clinical signs requiring medical treatment. Not expected to be life threatening with appropriate care.
  - Tea Tree Oil (melaleuca)
  - Nicotine patches
  - Pyrethrins
  - Fentanyl patches

- **Major**: Will cause signs that, if left untreated, will likely result in permanent organ damage or death.
  - 5-Fluorouracil (5-FU)
  - Salicylates (aspirin)
  - Dovonex (vitamin D₃)
Other than stains on the carpet, there’s little to fear.

ZINC OXIDE
Zinc Oxide Ointment: MINOR

- Sources
  - Diaper rash creams (Desitin®, 20-40%)
  - Generic “skin protectants”
  - Sunscreen

- MOA: Strong gastric irritant (former emetic)

- Elemental zinc toxicity is not expected
Zinc Oxide Ointment: MINOR

• Clinical Signs:
  – Spontaneous vomiting (very common)
  – +/- diarrhea

• Treatment
  – Symptomatic and supportive care
  – Fluid therapy
  – Anti-emetics (e.g., maropitant, etc.)
  – AC unlikely to be effective
    • Do not administer A/C
Zinc Oxide Ointments: The exception

• One Case Report:
  – Elemental zinc toxicosis following *chronic, massive* ingestion of ointment
  – Signalment: 6 yo, MC, 24.6 kg, Shetland sheepdog
  – PC: Rectal mass removal
  – Exposure:
    • Frequent application/ingestion of 40% Desitin® cream over 4 days
    • Ingestion of ¾ lbs of cream or 4,000 mg/kg of Zn
  – Clinical Signs:
    • Day 4: Lethargy, hematuria, icterus, ↑ serum Zn levels
  – Complete recovery following multiple blood transfusions and aggressive care

Commonly encountered—uncommonly problematic.

STEROIDS AND ANTIBIOTICS
Topical Steroids and Antibiotics: MINOR

• Source:
  – OTC creams/ointments, ophthalmic products
    • Steroids: 1 % hydrocortisone, betamethasone, or triamcinolone
    • Antibiotics: neomycin sulfate, bacitracin, and polymyxin sulfate (i.e. Neosporin® and generic “triple antibiotic”)
  • Rule out topical NSAIDs – more dangerous and potent!

• Clinical Signs:
  – GI: mild, self-limiting vomiting and diarrhea
    • Petroleum-based carrier = laxative
  – Renal: possible mild PU/PD
Topical Steroids and Antibiotics: MINOR

• Treatment
  – Symptomatic and supportive care
  – Outpatient therapy
    • Fluid therapy
    • Anti-emetics (e.g., maropitant, ondasetron, etc.)
  – No need to administer A/C
Shake, shiver and roll...

PYRETHRINS & PYRETHROIDS
Pyrethrins/Pyrethroids: MINOR (dog) to MODERATE (cat)

• Common topical canine flea/tick treatment
  – Squeeze-on, 40-45% concentration
  – (Shampoo, powder, home insect sprays, <1%, not an issue)

• Cats are FAR MORE sensitive than dogs!
  – Metabolized via glucuronidation
  – Cats—develop toxicity at 5-10% permethrin
  – Cats who groom dogs are at risk too
Pyrethrins/Pyrethroids: Clinical signs

• Dogs: often related to paresthesia
  • Don’t confuse with systemic toxicity!
  • Not an “allergic” reaction
  • Clinical signs: agitation, nervousness, skin twitch
  • Typically not primary redness or inflammation (secondary to trauma and pruritis)
  • Vomiting and salivation common with ingestion

• Cats: systemic toxicity
  • Facial twitching, ear flicking, whole body “twitches,” tremors, seizures
Pyrethrins/Pyrethroids—treatment

• Stabilize, then decontaminate

• Cats
  – Methocarbamol!!
    • High doses OK (150-250 mg/kg)
    • Give IV slow, to effect (oral too slow)
  – Diazepam – typically poor response
  – IV fluids, monitor renal values (if prolonged tremors)

• Dogs
  – Think paresthesia, not systemic toxicity
  – Bathe in cool water (dish soap)
  – Vitamin E oil to application site PRN x 1-3 days
TEA TREE (MELALEUCA) OIL

Not your mother’s tea party...
Tea Tree Oil (*Melaleuca*): MODERATE

- Source—extract from Australian tea tree leaves
  - Found as 100% oil or diluted into antiseptics, face washes, anti-parasite products

- MOA: Unknown
  - Rapidly absorbed from the skin or GI tract
Tea Tree Oil (*Melaleuca*): MODERATE

- **Toxic dose:** < 10 mls on dogs or cats

- **Clinical signs:**
  - Weakness, CNS depression, ataxia, tremors, hypothermia, hepatotoxicity (rare)
  - Characteristic odor on pet’s fur!
  - Time to onset: 2-8 hrs
  - Time to resolution: 1-2 days
Tea Tree Oil (*Melaleuca*): MODERATE

- **Treatment**
  - **Decontamination:**
    - Bathe with a de-greasing detergent (dish soap)
    - Flush out of ears
    - Activated charcoal
      - Even with *dermal* toxicosis?
  - Supportive care: IV fluids, thermal support, monitor LES
  - Intravenous lipid emulsion (ILE)?
More than just a smoker’s buzz.

NICOTINE PATCHES
Nicotine Patches: MODERATE

- **Source**
  - Brands: Nicoderm®, Habitrol®, Leader®, Nicotinell®
  - Each patch: 7-50 mg nicotine
    - 1 unfiltered cigarette: ~12 mg
  - Used patches contain nicotine too

- **Toxic dose**
  - Canine LD$_{50}$ (oral): 9-12 mg/kg

- **MOA/pharmacology:**
  - Binds to nicotinic cholinergic receptors
  - CNS stimulant then depressant
  - Rapidly and completely absorbed from the GIT
Nicotine Patches: MODERATE

• Time Frame
  – Onset of action: 15-60 min
  – Duration of signs: Hours to days
  – GI transit time of patch: 25-57 hours (experimental dogs)

• Clinical Signs
  – Early signs:
    • GI: Salivation, vomiting
    • CNS: Hyperexcitability, mydriasis, tremors
    • CARDIAC: Tachycardia, tachypnea, hypertension
  – Following the hyperexcitable phase, may see seizures and death
  – Delayed: CNS depression, ataxia, respiratory depression
Nicotine Patches: MODERATE

• Treatment
  – Treatment typically focused on clinical signs vs. patch removal
  – If ASX: decontamination:
    • Emesis (if not vomiting)
    • Activated charcoal with a cathartic 1X
  – Supportive care

• Contraindications (DO NOT GIVE!)
  – Antacids (may ↑ gastric absorption)
  – No H₂ blockers!
More narc for your buck.

FENTANYL PATCHES
Fentanyl Patches: MODERATE

• 50-100X more potent than morphine
• Patch, when chewed, release drug
• “Spent” patches as up to 84% of original fentanyl

• Source
  – Patch ingestion
  – Iatrogenic toxicity during surgery (heat ↑ excretion)
Fentanyl Patches

• Rapid onset of signs
  – Dogs: Sedation, CNS depression, cardiac/resp depression, miosis, hypothermia
  – Cats: Paradoxical CNS stimulation and mydriasis

• Death due to resp. depression (rare)

• Decontaminate?
  – Emesis:
    • Only if quickly after ingestion
    • If ASX
  – Endoscopic retrieval of patch
Fentanyl Patches: MODERATE

- Opioid reversal: naloxone
  - Inexpensive!
  - Dose: 11-44 mcg/kg IV, IM, or SC
  - Repeat, repeat, repeat!
  - Wide margin of safety

- Don’t have naloxone?
  - Consider torbugesic 0.1 mg/kg IV, IM for partial reversal

- Supportive care
  - Thermal support
  - Treatment for bradycardia
    - Atropine: 0.01-0.02 mg/kg IV, IM
    - Glycopyrrolate: 0.01-0.02 mg/kg IV, IM
  - Ventilation
  - Diazepam for seizures
Took two of these? Call me right away!

SALICYLATES
Acetylsalicylic acid (aspirin or ASA):
- Acne control creams, masks, pads, face washes, and make-up (Clearasil®, Noxzema®)
- Concentration 1-5%

Methylicsalicylate:
- Linaments (BenGay®, HEET®)
- 18-30%
- Oil of wintergreen
  - 1mL of oil is equivalent to 1.4 grams of aspirin
  - 1 teaspoon (5 mL) is equivalent to 21.5 adult aspirin tablets (325 mg)!
  - 1 tsp has lead to children’s death

Salicylates: MODERATE TO MAJOR

PET POISON HELPLINE
Salicylates: MOA/Pharmacology

• Inhibits COX which causes reduction in prostaglandins and thromboxanes
• Irreversible effect on platelet aggregation
• Uncouples oxidative phosphorylation resulting in hyperthermia
• Rapidly absorbed from stomach and upper small intestine
• Excreted via kidneys both by filtration and tubular secretion
• $T_{1/2}$:
  – Dogs = 7.5 to 8 hours
  – Cats = 38-45 hours
Salicylates: Range of toxicity

• Dogs:
  – Up to 75 mg/kg have resulted in signs of GI distress
  – 100-300 mg/kg should be referred to the clinic
  – >300 mg/kg need full and aggressive treatment
  – >400 mg/kg have resulted in death and carry a poor prognosis
  – >500 mg/kg carry an extremely poor prognosis

• Cats:
  – Anything over 25-30 mg/kg is generally felt to be a toxic dose

But do you know how to calculate it?
Salicylates: Clinical signs

• **Common** (start 4-6 hrs post ingestion)
  – GI—vomiting (hematemesis), melena
  – Hyperthermia
  – Respiratory—tachypnea
  – CNS—lethargy, weakness, depression, ataxia, coma
  – Acid/base—early respiratory alkalosis followed by a **severe** metabolic acidosis

• **Less frequent**
  – GI—gastric perforation
  – Hematopoietic—anemia, thrombocytopenia, bone marrow suppression, Heinz bodies (cats)
  – Respiratory—pulmonary edema
  – Renal failure and/or centrilobular liver necrosis
Salicylates: Treatment

- **Antidote:** None
- **Decontamination:**
  - Emesis induction?
  - Activated charcoal/cathartic (ACC) X1
- **Fluid therapy:** IV fluids
  - Maintain renal vasodilatation
- **GI protectants** x 10-14 days
- **Cooling measures** (do not cool below 103.5°F)
- **Sodium bicarbonate**—may increase elimination
- **Diazepam** for seizures
- **Blood or plasma transfusions**
- **Vitamin K₁** for prolonged coagulation
Better known as “5-FU”....which is quite close to what you’ll want to say.

5-FLUOROURACIL (5-FU)
5-Fluorouracil (5-FU): MAJOR

• Source
  – Rx anti-neoplastic, 0.5-5%
    • Superficial basal cell carcinomas and actinic keratosis (humans)
    • Limited topical and IV use in veterinary medicine
  – Brand names
    • Efudex®, Carac®, Adrucil®, Fluoroplex®
5-Fluorouracil (5-FU): MAJOR

- Inhibits DNA and RNA synthesis and production
- Rapidly absorbed from GIT
- Toxicity:
  - Cats: Even very small amounts may cause CNS signs
  - Dogs:
    - 8.6 mg/kg = minimum reported toxic dose
    - 20 mg/kg = minimum reported lethal dose
    - 46 mg/kg = ONE dog survived this dose!
      - This is only 1/2 of a 40 gm (5%) tube in a 50 lb dog!
- Prognosis
  - Cats = grave (any amount)
  - Dogs = guarded to poor, ~25% survival rate
5-Fluorouracil (5-FU): MAJOR

- **Onset of action**
  - 1-5 hr
  - Death within 7 hours

- **Clinical Signs**
  - Persistent vomiting
  - Sloughing of the GIT
  - Multi organ failure
  - Severe and non-responsive seizures
  - Dose dependent myelosuppression (pancytopenia)
  - Death
5-Fluorouracil (5-FU): MAJOR

- **Treatment**
  - **ANTIDOTE:** Uridine triacetate (Orphan Drug, available on a per patient basis)
    - Anecdotally less effective in dogs. More info: ClinicalTrials.gov, type in “5FU overdose”
  - Emesis not typically advised (already symptomatic)
  - Baseline blood work (e.g., CBC, chemistry, venous blood gas)
  - Manage hypovolemia (IV crystalloids)
  - Gastrointestinal support: GI protectants, anti-emetics
  - Seizures—non-responsive to diazepam
    - Aggressive anticonvulsant therapy:
      - Barbiturates, propofol, gas anesthesia
  - If leukopenic (<1000 X 10³/µl), consider antibiotics
  - Anxiolytics?

- **Monitor**
  - CBC every 3-4 days for at least 18 days
    - RBCs, WBCs, platelets continued to drop through day 13
    - Cell lines returned to normal by day 25
Caught between a rock and a hard place.

CALCIPOTRIENE
Calcipotriene: MAJOR

• Source
  – Vitamin D analogue
  – Topical psoriasis treatments
  – Dovonex® (calcipotriene) cream or solution
    • 0.005% or 50 mcg/gm
    • Packaged 60 and 120 gram aluminum tubes
  – Taclonex® (calcipotriene and betamethasone)
    • Calcipotriene: 50 mcg/gm
      Betamethasone: 0.5 mg/gm
Calcipotriene: MAJOR

• Promotes calcium retention
  – ↑ Ca and phos absorption from the GIT
  – ↑ Ca reabsorption from the distal tubules
  – ↑ Ca mobilization from the bones

• Toxicity results in
  – Hypercalcemia (total serum calcium and iCa)
  – Hyperphosphatemia
  – Metastatic tissue calcification

• Enterohepatic recirculation occurs
Calcipotriene: MAJOR

• Range of Toxicity
  – Minimum acute toxic dose (dogs): 37 mcg/kg
  – Chronic
    • 3.6 mcg/kg/day x 1 week in dogs=
      ↑ Ca, ↑ Phos, ↑ BUN & creatinine
  – Cats: unknown but more sensitive
Calcipotriene: MAJOR

- Clinical Signs
  - Onset in 8-24 hrs
  - GI: anorexia, vomiting, +/- GI ulceration
  - CNS: depression, weakness
  - Renal: PU/PD, dehydration, isosthenuria, azotemia
  - Cardiac changes (rare)
Treatment

• Promote calciuriesis!
  • Aggressive 0.9% NaCL diuresis
  • Furosemide
  • Dexamethasone or prednisone

• Inhibit bone resportion: Pamidronate (Aredia)
  • Bisphosphonate drug

• Decrease phosphorous:
  • Oral phosphate binders (aluminum hydroxide)

• Gastrointestinal support:
  • GI protectants as needed
  • Anti-emetics

• Antidote: Intravenous lipid emulsion?
Calcipotriene: MAJOR

- Treat for 2-3 weeks!

- Labs
  - Repeat Ca, phos, BUN, creatinine q 12-24 hours.
  - Phos rises before Ca (indicator of poisoning)
  - Long-term monitoring q. 2-5 days

- Prognosis
  - Good if treatment is started before hypercalcemia
  - Guarded to poor if:
    - Soft tissue mineralization
    - Gastric ulceration
    - Dyspnea (lung mineralization)
When in doubt, call for the bad ones

• Something you’re not familiar or comfortable with
• Human drugs
  • Mixed drug ingestions
  • Severe clinical signs
  • Animals with preexisting disease
Did you get your “wheel of vomit”?

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Baby Products Poisonous to Pets
Speakers: Justine A. Lee, DVM, DACVECC, DABT
          Ahna G. Brutlag, DVM, MS, DABT
Date: April 9, 2013
Time: 12-1 pm CST (1-2pm EST)

Top 10 Toxins Poisonous to Small Animals
Speakers: Justine A. Lee, DVM, DACVECC, DABT
          Ahna G. Brutlag, DVM, MS, DABT
Date: October 8, 2013
Time: 12-1 pm CST (1-2pm EST)

Topical Toxins Poisonous to Pets
Speakers: Justine A. Lee, DVM, DACVECC, DABT
          Ahna G. Brutlag, DVM, MS, DABT
Date: June 4, 2013
Time: 12-1 pm CST (1-2pm EST)

Holiday Dangers Poisonous to Pets
Speakers: Justine A. Lee, DVM, DACVECC, DABT
          Ahna G. Brutlag, DVM, MS, DABT
Date: December 3, 2013
Time: 12-1 pm CST (1-2pm EST)

Register at www.petpoisonhelpline.com/veterinarians/webinars

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