

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

#### PET POISON HELPLINE



## Topical Toxins Poisonous to Pets

Ahna Brutlag, DVM, MS, DABT Assistant Director, Pet Poison Helpline abrutlag@petpoisonhelpline.com

Justine A. Lee, DVM, DACVECC, DABT Associate Director, Pet Poison Helpline jlee@petpoisonhelpline.com





# Introduction



Ahna G. Brutlag, DVM, MS, DABT

#### **Assistant Director**

Pet Poison Helpline Minneapolis, Minnesota





## Introduction



Justine A. Lee, DVM, DACVECC, DABT

**Associate Director** 

Pet Poison Helpline Minneapolis, Minnesota





#### VPI<sup>®</sup> and Pet Poison Helpline<sup>®</sup> 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<sup>®</sup> and Pet Poison Helpline<sup>®</sup> working together

Providing veterinary reviewed pet health information online

- www.petpoisonhelpline.com/owners
- www.petinsurance.com/healthzone.aspx  $\succ$
- 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



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# 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
    - PharmDs/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  $D_3$ )





Other than stains on the carpet, there's little to fear.

### **ZINC OXIDE**





# Zinc Oxide Ointment: MINOR

- Sources
  - Diaper rash creams (Desitin<sup>®</sup>, 20-40%)
  - Generic "skin protectants"
  - Sunscreen
- MOA: Strong gastric irritant (former emetic)
- Elemental zinc toxicity is <u>not</u> 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<sup>®</sup> cream over 4 days
    - Ingestion of <sup>3</sup>/<sub>4</sub> lbs of cream or 4,000 mg/kg of Zn
  - Clinical Signs:
    - Day 4: Lethargy, hematuria, icterus,  $\uparrow$ serum Zn levels
  - Complete recovery following multiple blood transfusions and aggressive care

# **STEROIDS AND ANTIBIOTICS**

Commonly encountered—uncommonly problematic.









## **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<sup>®</sup> 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)</li>
- 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





Not your mother's tea party...

# TEA TREE (MELALEUCA) OIL





### Tea Tree Oil (*Melaleuca*): MODERATE

- Source—extract from Australian tea tree leaves
  - Found as 100% oil or diluted into antiseptics, face washes, antiparasite 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<sup>®</sup>, Habitrol<sup>®</sup>, Leader<sup>®</sup>, Nicotinell<sup>®</sup>
  - Each patch: 7-50 mg nicotine
    - 1 unfiltered cigarette: ~12 mg
  - Used patches contain nicotine too
- Toxic dose
  - Canine LD<sub>50</sub> (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

15-60 min

- Time Frame
  - Onset of action:
  - 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  $\uparrow$  gastric absorption)
  - No H<sub>2</sub> 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
  - latrogenic toxicity during surgery (heat  $\uparrow$  excretion)



#### **Fentanyl Patches**



- 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





# Salicylates: MODERATE TO MAJOR

- Acetylsalicylic acid (aspirin or ASA):
  - Acne control creams, masks, pads, face washes, and make-up (Clearasil<sup>®</sup>, Noxzema<sup>®</sup>)
  - Concentration 1-5%
- Methylsalicylate:
  - Linaments (BenGay<sup>®</sup>, HEET<sup>®</sup>)
  - 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: 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<sub>1/2</sub>:
  - 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?







- GI—vomiting (hematemesis), melena
- Hyperthermia
- Respiratory—tachypnea
- CNS—lethargy, weakness, depression, ataxia, coma
- Acid/base—early respiratory alkalosis followed by a <u>severe</u> 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 K<sub>1</sub> for prolonged coagulation





Better known as "5-FU"....which is quite close to what you'll want to say.

## 5-FLUOROURACIL (5-FU)





- 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<sup>®</sup>, Carac<sup>®</sup>, Adrucil<sup>®</sup>, Fluoroplex<sup>®</sup>





- 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





- Onset of action
  - 1-5 hr
  - Death within7 hours
- Clinical Signs
  - Persistent vomiting
  - Sloughing of the GIT
  - Multi organ failure
  - Severe and non-responsive seizures
  - Dose dependent myelosuppression (pancytopenia)
  - Death





- 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 10<sup>3</sup>/ 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





- Source
  - Vitamin D analouge
  - Topical psoriasis treatments
  - Dovonex<sup>®</sup> (calcipotriene) cream or solution
    - 0.005% or 50 mcg/gm
    - Packaged 60 and 120 gram aluminum tubes
  - Taclonex<sup>®</sup> (calcipotriene and betamethasone)
    - Calcipotriene: 50 mcg/gm Betamethasone: 0.5 mg/gm





### Promotes calcium retention

- $\uparrow$  Ca and phos absorption from the GIT
- $\uparrow$  Ca reabsorption from the distal tubules
- $\uparrow$  Ca mobilization from the bones

### • Toxicity results in

- Hypercalcemia (total serum calcium and iCa)
- Hyperphosphatemia
- Metastatic tissue calcification

• Enterohepatic recirculation occurs





- 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





- 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?





- 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

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

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## Vet tox textbook!







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#### ALL LECTURES ARE 1 HOUR OF FREE CE

#### **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 IOTOXINS 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)

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