COMMON TOXICITIES

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Overview

- Decontamination
  - Emesis
  - Gastric lavage
- RRT
- ILE

Overview

- Toxins
  - MOA
  - Clinical signs
  - Diagnosis
  - Treatment
Emesis

Recommended within 2 hours of ingestion of toxic product

Emesis

- Contraindications:
  - Ataxia
  - Coma
  - Seizures
  - Hyperactivity
  - Corrosive materials
  - Petroleum
  - Pet previously vomited

Emesis

- Contraindications
  - Ingestion of drug with substantial antiemetic properties
  - Pet with increased risk of aspiration pneumonia
Apomorphine

- **MOA:**
  - Centrally active nonselective dopamine agonist
  - Direct stimulation of CRTZ
  - Depresses vomiting center in the medulla
    - Second dose not recommended

Plumb’s Veterinary Drug Handbook 7th edition

Apomorphine

- **Administered**
  - IV, SQ, IM or conjunctival membranes
  - Not effective orally
    - Due to high first pass hepatic metabolism
    - Slow absorption

- **Dose**
  - 0.03-0.04 mg/kg

Plumb’s Veterinary Drug Handbook 7th edition

Apomorphine

- **Side effects**
  - Reddened eye (conjunctival administration)
  - Lethargy
  - Persistent nausea
  - Hypersalivation
3% Hydrogen Peroxide

MOA:
- Local stimulation of nerve endings in GIT transmitted to vomiting center through vagal nerve

ASPCA Animal Poison Control

3% Hydrogen Peroxide

Administered orally
- Dose 2.2 ml/kg (maximum dose 45 ml/dog)

ASPCA Animal Poison Control

3% Hydrogen Peroxide

Adverse Effects
- Diarrhea
- Lethargy
- Protracted signs of nausea and vomiting

ASPCA Animal Poison Control
ASPCA Poison Control paper

Effectiveness and adverse effects of the use of apomorphine and 3% hydrogen peroxide solution to induce emesis in dogs.

JAVMA Vol. 241 No. 9 Nov 1, 2012

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ASPCA Poison Control paper

- 147 dogs
- Both were effective when used as directed
- Emesis occurred within minutes
- Side effects mild and self-limiting

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ASPCA Poison Control paper

No significant difference if vomiting induced by vet, staff member, clinician or at home
ASPCA Poison Control paper

- Apomorphine
  - Improper mixture, storage or stability of product, different manufactures influence on effect was not considered
  - Accurate dosing of conjunctival product difficult to determine

ASPCA Poison Control paper

- 3% Hydrogen Peroxide
  - Use of hydrogen peroxide beyond expiration date could reduce efficacy, this information was not recorded.

ASPCA Poison Control paper

- Overall both products very effective
- 3% Hydrogen Peroxide PO
- Apomorphine IV or conjunctival sac
- Advisable clients consult with veterinary professional prior to administering 3% hydrogen peroxide at home.
**Gastric Lavage**

- **Recommended:**
  - Within 2 hours of ingestion of toxin
  - Unable to induce vomiting
    - Mentally altered
    - Emesis unsuccessful

- **RRT**
  - Renal replacement therapy
    - Intermittent hemodialysis (IHD)
    - Continuous renal replacement therapy (CRRT)
IHD

- Typically provided for 3-6 hrs per day
- Generally 3 times per week
- Can be done on consecutive days

CRRT

- Provides slower and continuous rate of solute and water removal
- Sessions approaching 24 hrs per day

RRT

- Toxin requirement
  - Small size particle
  - Poorly protein bound
  - Small volume of distribution
RRT
- Uses
  - AKI
  - Toxicities
  - Fluid overload
  - CHF
  - Immune mediated disease

ILE
- Intravenous lipid emulsion
- Part of parenteral nutrition formulation

ILE
- MOA
  - Exact MOA is unknown
  - May have more than 1 MOA
  - Lipid sink

The use of ILE as an antidote in vet. toxicology, JVECCS, 21(4) 2011, 309-320
**ILE**

- **Lipid sink**
  - Toxic compound is sequestered into the lipid compartment within the blood stream
  - Only useful with lipophilic drugs

The use of ILE as an antidote in veterinary toxicology, *JVECCS*, 21(4) 2011, 309-320

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**ILE**

- **Adverse effects**
  - Contamination of product resulting in:
    - Local or systemic infection
    - Venous irritation
    - Thrombophlebitis

The use of ILE as an antidote in veterinary toxicology, *JVECCS*, 21(4) 2011, 309-320

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**ILE**

- **Adverse effects**
  - Fat overload syndrome (FOS)
    - Generally delayed or subacute
    - Related to overdose or pets with decreased plasma clearance of lipids
    - Fat embolism, hyperlipidemia, hepatomegaly, icterus, splenomegaly, thrombocytopenia, hemolysis, increased clotting times

The use of ILE as an antidote in veterinary toxicology, *JVECCS*, 21(4) 2011, 309-320
ILE

- Hypertriglyceridemia and lipemia are unavoidable
- No cause and effect between pancreatitis and transient hypertriglyceridemia

The use of ILE as an antidote in vet. toxicology, JVECCS, 21(4) 2011, 309-320

ILE

- Dose:
  - Bolus between 1.5-4 ml/kg over 1 minute
  - CRI 0.25 ml/kg/min over 30-60 min

The use of ILE as an antidote in vet. toxicology, JVECCS, 21(4) 2011, 309-320

Rodenticide toxicity

Anticoagulant

- MOA
  - Inhibition of K1 epoxide reductase
  - This enzyme reduces Vit. K1 2,3 epoxide to Vit K1
  - Vit K1 is needed to synthesize clotting factors II, VII, IX & X
Rodenticide toxicity
Anticoagulant

- Depletion of Vit. K1 in the liver results in clinical coagulopathy
- Plasma 1/2 life of clotting factors
  - Factor II: 41 hours
  - Factor VII: 6.2 hrs
  - Factor IX: 13.9 hrs
  - Factor X: 16.5 hrs

Can see lag time of 3-5 days between ingestion of rat bait and clinical signs.

First generation VS second generation
First generation Anticoagulant Rodenticide toxicity
- Moderate toxicity
- LD₅₀ 10-50 mg/kg
- Require continuous bait exposure
- Many rodents have developed resistance

Second generation Anticoagulant Rodenticides
- Superwarfarins
- LD₅₀ 0.2-3.9 mg/kg
- Ex: bromadiolone, brodifacoum, diphacinone, chlorphacinone

Second generation Anticoagulant Rodenticides
- Greater potency & longer duration of action
  - Greater affinity for Vit. K₁-2,3 epoxide reductase
  - Ability to inhibit Vit. K₁ cycle at more than 1 point
  - Hepatic accumulation
  - Long ½ life due to lipid solubility and enterohepatic circulation
Toxicity

- Most common rodenticide toxicity exposure in dogs
- Most common accidental
- Intentional

Diagnosis

- History of ingestion
- Clinical signs
- Coagulopathy

Clinical signs

- Depression
- Weakness
- Dyspnea
- Pallor
- Ventral hematoma
- Anorexia
Clinical signs

- Pulmonary edema
- Pleural effusion
- Pericardial effusion
- Intracranial hemorrhage
- Laryngeal obstruction

Coagulopathy

- Reduced activity of factors II, VII, IX & X
- OSPT (PT) evaluates factor VII
  - Most sensitive
  - Factor VII has shortest $\frac{1}{2}$ life (6.2 hours)
  - APTT tests everything but factor VII

Therapy

- Induce vomiting if BAR
- Gastric lavage
- Activated charcoal
Therapy

- Vitamin K: 0.25-2.5 mg/kg PO SID or divided BID X 1 week for short acting rodenticides
- Vitamin K 2.5-5.0 mg/kg PO SID or divided BID X 3-4 weeks for longer acting rodenticides
- If type unknown treat 3-4 weeks
- Recheck PT 48 post stopping Vit. K

Therapy

- Fresh plasma
- pRBC or whole blood transfusion
- Vitamin K SQ, (IV associated with anaphylaxis)
- O2
- IVF

Non-anticoagulant rodenticides

- Bromethalin
Bromethalin

- Developed for use against warfarin-resistant rodents
- Very toxic requires only one dose
- Can not be distinguished from rodent baits by color or appearance
- Secondary toxicity can result from ingestion of mouse/rat killed by bromethalin

Bromethalin MOA

- Uncouples oxidative phosphorylation in the mitochondria = decreased ATP synth
- Decreased energy to fuel Na,K ATPase pumps
- Loss of cellular osmotic control, cell swelling

Bromethalin MOA

- Fluid accumulation within myelin sheaths
- Decreased nerve conduction
- Increased ICP
  - Convulsions
  - Paralysis
  - Death
Bromethalin

Clinical signs occur with 10 hours to several days after exposure and can last up to 12 days.

- Change in mental status
- Hind limb paralysis
- Severe muscle tremors
- Hyper excitability
- Hyperesthesia
- Hypertermia
- Cyanosis

Bromethalin diagnosis

- History of exposure
- Clinical signs
### Bromethalin Treatment
- No specific antidote
- Emesis if BAR/gastric lavage
- Activated charcoal
- Antiseizure meds.
- Mannitol
- IVF
- Artificial ventilation
- Corticosteroids???

### Ivermectin
Potent antiparasitics against almost all parasites except trematodes and cestodes

### Ivermectin
- Approved for use in dogs, cats, sheep, horses, cattle and reindeer
- Not approved in lactating animals
- Puppies and kittens younger than 6 wks
Ivermectin

- Absorbed subcutaneously and orally
- Rapid GI absorption
- Peak plasma levels in 2-4 hours
- Metabolized in the liver via oxidation
- Excreted in bile to feces.
- <5% excreted in urine
- ½ life 2 days in dogs

Ivermectin

- Dose: 2 mg/kg PO as a single dose (dogs)
  - 0.2-1.3 mg/kg PO/SQ cats
  - LD50: 80 mg/kg

Ivermectin toxicity

- MDR1-allele mutation (Aussie shep., shelties, long haired whippet, “white feet”)
  - Toxic dose 100-500 mcg/kg
- Crosses BBB
- Effects GABA-gated chloride channels and hyperpolarization of cell membranes
**Ivermectin**

- Clinical signs
  - Bradycardia
  - Respiratory depression
  - Cyanosis
  - Mydriasis
  - Blindness
  - Vomiting
  - Ataxia
  - Tremors
  - Hypersalivation
  - Coma
  - Death

**Ivermectin**

- Treatment
  - No specific antidote
  - If oral ingestion emesis/gastric lavage
  - Symptomatic/supportive care
  - Recovery: slow, up to 5-7 days
    - Some require care for 3-5 weeks

**Ivermectin**

- ILE therapy
  - Bolus 1.5 ml/kg
  - CRI 0.25 ml/kg/min over 30-60 min
  - Can repeat in 4 hours
Organophosphates

- Common pesticides used in agriculture, industry and home/garden
- Gain entry to the body via oral, dermal or inhalation

**Organophosphates**

- **ACHe inhibitor**
  - Overstimulation of the post-synaptic neuron or muscle
- Clinical signs occur within 15 min to 1 hour of exposure

Organophosphates

Clinical signs include muscarinic, nicotinic, and central nervous signs
Organophosphates clinical signs

- Muscrinic
  - Vomiting
  - Abdominal and chest pain
  - SLUD (salivation, lacrimanition, urination, defecation)
  - Miosis
  - Pulmonary edema
  - Cyanosis

Organophosphates clinical signs

- Nicotinic
  - Muscle twitching
  - Seizures
  - +/- paralysis

Organophosphates clinical signs

- Central
  - Restlessness
  - Ataxia
  - Neck stiffness
  - Coma
  - Death secondary to respiratory and/or cardiac arrest
Organophosphates treatment
- Before instituting antidotal therapy gastric lavage should be performed
- Activated charcoal
- Bath animal with dermal exposure

Organophosphates treatment
- Atropine sulfate
- Mainstay of treatment
- Addresses muscarinic signs: bradycardia and excessive bronchial secretions
  - 0.1-2 mg/kg (1/4 dose IV, rest SQ)
  - Repeat 0.1-0.25 mg/kg IV q 20-30 min. until muscarinic signs resolve.

Organophosphates treatment
- 2-PAM (pyridine-2-aldoxime methochloride)
- Antidote for nicotinic signs
- Little effect on muscarinic and CNS signs
- Must use atropine!!
- Dose:
  * 10-20 mg/kg SQ or IV (slow) q 12 hours.
Organophosphates
2-PAM (pyridine-2-aldoxime methochloride)
- Contraindicated in subacute or chronic cases
- OP molecules become permanently attached to AchE
- Anticholinesterase properties predominate

Pyrethrins
- Insecticides
- Obtained from Chrysanthemum
- Applied dermally
  - Grooming: oral
  - Inhalation

Pyrethrins
- Type I or T-syndrome (tremor)
  - Increased sens. to stimuli
  - Fine tremors
  - Clonic seizures
  - Abnormal hind limb movements
  - Hypothermia
Pyrethrins

- Type II- CS-syndrome (CNS)
  - Pawing
  - Burrowing
  - Salivation
  - Coarse tremors
  - Jerky uncontrolled excessive movements

- Presence of alpha-cyano group on the Type II compounds

Pyrethrins

MOA

- Primarily voltage sensitive Na. channels
- Type I compounds
  - Cause repetitive firing of action potentials
- Type II compounds
  - Cause extended depolarization due to prolonged opening of the channels
Pyrethrins

MOA

- Other interactions: Type II compounds
  - Peripheral and central GABA receptors
  - Seizure activity

Pyrethrins

- Treatment
  - No specific antidote
  - Wash animal
  - Emetics/gastric lavage
  - Activated charcoal
  - Antiseizure medication (diazepam, Phenobarbital)
  - ILE
  - Muscle relaxants (methocarbamol 50 mg/kg IV. Do not exceed 330 mg/kg/day)

Zinc

- Most common source pennies (minted after 1983), galvanized metallic hardware and zinc oxide.
- MOA: not well defined
Zinc

- **Clinical signs**
  - hemolytic anemia
  - gastroenteritis

- **Diagnosis**
  - Radiographic evidence
  - Pepto bismol

- **Treatment**
  - Removal of the source
  - Supportive care:
    - Blood transfusion
    - IVF
    - Antiemetic
    - GI protectants
    - Monitor PCV, platelets and chemistry profile
Zinc chelation

- Measure zinc level if possible
- Normal 0.06-0.2 mg/dL
- Calcium disodium EDTA 100 mg/kg divided into 4 doses per day, SQ, 25 mg/kg divided into 4 doses SQ X 5 days.
- Duration of treatment is unclear.
- Adverse effects renal tubular necrosis

Xyiltol

- Five carbon sugar alcohol used as a sugar substitute
- Contained in gum, candy, baked goods, PB toothpaste, ect.
- Toxic dose 0.15 g/kg

Xylitol

- Hypoglycemia
  - Due to massive insulin release
- Hepatic necrosis
- Coagulopathy
- DIC
**Xylitol**

- Some dogs develop increased L.E. 8-12 hours post ingestion and recover fully
- Others develop acute hepatic failure and never develop hypoglycemia

**Treatment**

- Induce vomiting
- Activated charcoal does not bind xylitol
- Monitor BG and L.E.
  - BG q 2-4 hours
  - L.E. on presentation
  - 24, 48 and/or 72 hrs post based on presenting L.E.

**Ethylene glycol**

- Most common source antifreeze in automobiles
- Toxic dose:
  - Dogs: 4.2-6.2 mg/kg
  - Cats: 1.5 mg/kg
Ethylene glycol

- Rapidly absorbed from GI tract and reaches peak concentrations in 1-3 hours
- Metabolites of E.G. are responsible for severe acidosis and renal injury
- Metabolism is catalyzed by alcohol dehydrogenase

Ethylene glycol

- E.G. is a potent CNS depressant and GI irritant
- CNS depression within 30 minutes

Ethylene glycol

- Ethylene Glycol
- Glycoaldehyde
- Glycolic acid*
- Glyoxylic Acid *
- Oxalic acid*
**Ethylene glycol stages**
- **Stage 1:** duration ½ - 12 hours
  - Increased serum osmolality (> 400 mOsm/kg)
  - PU/PD
  - Vomiting
  - Animal appears intoxicated, stuporous
  - Tachypneic/tachycardia secondary to severe metabolic acidosis
  - Renal damage secondary to renal tubule Ca. oxalate precipitation and glycolate

**Ethylene glycol stages**
- **Stage 2:** occurs 12 - 24 hrs. post ingestion
  - Cardiopulmonary signs
    - Tachypnea
    - Tachycardia
    - Pulmonary edema
    - Heart failure

**Ethylene glycol stages**
- **Stage 3:** occurs 24 - 72 hours post ingestion in dogs. 12 - 24 hrs post ingestion in cats
  - Renal failure
    - Painful kidneys due to swelling, edema and necrosis.
Ethylene glycol diagnosis

- History of exposure
- Physical exam
- E.G. level in blood or urine
- Blood chemistries
  - Elevated serum osmolality
    - $2(Na) + (glucose/18) + (BUN/2.8)$
  - Severe metabolic acidosis
  - Low $iCa$. 
  - Ca. oxalate crystals in urine

Ethylene glycol treatment

- Decrease absorption
  - Emesis if patient BAR
  - Gastric lavage
  - Activated charcoal

Ethylene glycol treatment

- Prevention of metabolism
- Dogs:
  - 4-methylprazole (4MP)
    - Loading dose: 20 mg/kg IV
    - 12 hours post: 15 mg/kg IV
    - 24 hours post: 15 mg/kg
    - 36 hours post: 5 mg/kg
Ethylene glycol treatment

- Prevention of metabolism
  - Cats:
    - 4MP: 125 mg/kg IV slowly
    - 31.25 mg/kg IV at 12, 24, and 36 hours

  *USE IN CATS IS CONTROVERSIAL*

Ethylene glycol treatment

- Ethanol
  - 20%
  - CRI: 1 ml/kg/hr (maximum dose)
  - Recheck E.G. level in 24 hours

Ethylene glycol

RRT is an aggressive and effective tool to remove E.G. from blood stream. Ethanol and 4-MP are not antidotes.
**Ethylene glycol treatment**

- RRT
- IVF diuresis
- Place urinary catheter, monitor in/out
- Monitor electrolytes, BG, blood gas, osmolality
- Dopamine 3-5 mcg/kg/min CRI
- Furosemide CRI 0.1-1 mg/kg/hr

**Grapes/Raisins**

- Polyuric/oliguric/anuric renal failure within 72 hrs of ingesting grapes/raisins
- MOA/toxic principal unknown
- Histopath: proximal renal tubular degeneration, basement membrane intact.
- Mineralization of kidneys, gastric mucosa, myocardium, lung and blood vessels reported

**Raisins/Grapes**

- Lowest documented grape dose 0.7 oz/kg
- Lowest documented raisin dose 0.11 oz/kg
- Vomiting 6 hours post ingestion
- Progresses to anorexia and depression
Raisins/Grapes

- Treatment
  - Emesis/gastric lavage
  - Activated charcoal
  - IVF diuresis X 48 hrs
  - Monitor renal values/urine production
  - Symptomatic support for vomiting and diarrhea

- Normal renal values after 48 hours diuresis = good prognosis
- Development of oliguria/anuria ass. with poor prognosis

Polyurethane adhesives
- Gorilla glue
  - Gastric F.B.
  - Ingestion of 2oz has been sufficient
  - Polymerizes into a large friable gastric F.B
  - Evidence of F.B. seen on radiographs as early as 4 hrs post ingestion
Polyurethane adhesives
Gorilla glue
- Treatment
  - Surgery
  - Do not induce vomiting
  - Dilution with food or liquid will not prevent F.B.

Chocolate
- Theobromide: toxic ingredient in chocolate
  - LD₅₀: 250-500 mg/kg
  - 2/3-1 1/3 oz baking chocolate

Theobromide
- MOA
  - Antagonism of cell. adenosine recp.
  - Inhibit phosphodiesterase
  - Intracellular accum. of cyclic AMP
  - Interferes with uptake and store. of intracellular. Ca.
Chocolate

- MOA
  - CNS stimulation
  - Increased circulating catecholamines
  - Increased gastric secretions
  - Diuresis

Chocolate

- Clinical signs
  - Vomiting
  - Hyperactivity
  - Restlessness
  - Tachycardia
  - Tachypnea
  - Ataxia
  - Tremors
  - Seizures
  - Cardiac arrhythmias

Chocolate

- Treatment
  - No specific antidote
  - Emesis/gastric lavage
  - Activated charcoal
  - IVF
  - EKG
  - Seizure control
  - Catheterize bladder- methylxanthines are reabsorbed
Marijuana

- All parts of plant are toxic
  - Smoke, ingestion of products made with marijuana and concentrated THC and hashish oil
- CNS depressant
- Clients sometimes unwilling to admit
- Clients sometimes altered

Marijuana

- Active ingredient
  - $\Delta_9$-Tetrahydrocannabinol (THC)
  - Lipophilic
  - Metabolized in the liver
  - Dogs produce 8-OH-$\Delta_9$ THC
- MOA:
  - CNS depressant

Marijuana

- Diagnosis:
  - Hx of exposure
  - Clinical signs
  - Urine drug test
Marijuana

- Clinical signs
  - Depression
  - Hypothermia
  - Urinary incontinence
  - Bradycardia
  - Hyperesthesia
  - Mydriasis
  - Seizures
  - Hypothermia

Marijuana

- Treatment:
  - Supportive care
  - Monitor/treat for respiratory depression
  - Monitor/treat for seizures
  - ILE
  - Mechanical ventilation

Marijuana


- Conclusions
  - Significant correlation in number of medical marijuana licenses and marijuana toxicosis
  - Ingestion of baked good made with THC butter resulted in 2 deaths
  - UDST found unreliable
Marijuana

- Colorado
- CSU and Wheat Ridge Vet. Specialists
- 3 groups
  1. Dogs with a positive UDST, & known marijuana ingestion, known exposure, or highly suspected by the clinician or the client
  2. Dogs with neg. UDST and known ingestion
  3. Not tested with UDST and known ingestion

Evaluation of trends in marijuana toxicosis in dogs living in a state with legalized medical marijuana. JVECCS 22(6) 2012

Marijuana

- Significant correlation in number of medical marijuana licenses and marijuana toxicosis
  - Saw a 4-fold increase in cases
  - Not a controlled study
    - Clients more willing to admit toxicity because it is legal
    - Did not consider increase in Co. population of humans and dogs
    - Included 2 hospitals

Evaluation of trends in marijuana toxicosis in dogs living in a state with legalized medical marijuana. JVECCS 22(6) 2012

Marijuana

- Significant correlation in number of medical marijuana licenses and marijuana toxicosis
  - Not a controlled study
    - Potency of marijuana varies between plants
    - Medical marijuana more potent resulting in more clinical signs

Evaluation of trends in marijuana toxicosis in dogs living in a state with legalized medical marijuana. JVECCS 22(6) 2012
Marijuana

- Ingestion of baked good made with THC butter resulted in 2 deaths
  - 9yo MC Schipperke
  - Ingested 6 chocolate chip cookies made with medical marijuana butter
  - Found comatose by client 40 hours after ingestion
  - Clients declined gastric lavage
  - Received ILE
    - Bolus 2 ml/kg
    - CRI 4.1 ml/kg x 19 hrs


Marijuana

- 9yo MC Schipperke
  - Clients declined gastric lavage
  - Vomited at home
  - Received ILE
    - Bolus 2 ml/kg
    - CRI 4.1 ml/kg x 19 hrs
  - 38 hrs post admission developed coagulopathy
    - Ventral hematoma, epistaxis, hematemesis
  - Cardiac and resp arrest


Marijuana

- Ingestion of baked good made with THC butter resulted in 2 deaths
  - 7yo FS Cocker spaniel
  - 4hrs prior to presentation ingested 8" square pan of brownies made with medical grade THC butter
  - Gastric lavage and activated charcoal
  - Dog vomited at home
  - Hypoxia and arrest 10 hrs post admission

Marijuana

- Ingestion of baked good made with THC butter resulted in 2 deaths
  - THC LD50: 3000 mg/kg
  - Unlikely ingested this dose
  - Dogs more sensitive
  - THC butter contains add. toxic compounds
  - Higher concentration of THC
  - THC butter metabolized differently

Marijuana

- Ingestion of baked good made with THC butter resulted in 2 deaths
  - Ingestion of chocolate
    - 26 other dogs in study ingested similar products and survived
    - No clinical signs of chocolate toxicity reported
    - Other causes of death can not be ruled out, but marijuana toxicity considered a significant contributing factor.

Marijuana

- UDST found unreliable
  - UDST not validated for use in dogs
  - No validated screening test for dogs
  - False negatives
  - Tested too soon after exposure
  - Different metabolite in dogs
  - Handler error
  - Many different UDST available
Marijuana

- Overall
  - With the increase of medical marijuana may see increase in toxicities
  - Medical grade marijuana and metabolites stronger
    - More clinical signs
    - Require earlier, more aggressive therapy
  - UDST unreliable interrupt with caution


NSAIDs

- MOA
  - Cyclooxygenase-2 (COX 2) inhibitors selectively targets COX2 enzyme responsible for inflammation and pain.
    - Meloxicam, carprofen, deramaxx, acetaminophen
  - Cyclooxygenase-1 (COX 1) inhibitors effect production of prostaglandins and thromboxanes
    - Aspirin, ibuprofen
  - Nonselective cox inhibitor
    - Naproxen

- NSAIDs

- MOA:
  - Inhibition of prostaglandin production
    - Causes: gastric irritation/ulcers
    - Decreased renal profusion
**NSAIDS**

- **MOA**
  - Hepatic toxicity
    - Increased concentration of drugs in hepatobiliary compartment
    - Creation of reactive metabolites that cause oxidative stress
    - Mitochondrial damage

- **Clinical signs:** secondary to GI ulcer, GI perforation, renal failure, and/or hepatic toxicity:
  - Anorexia
  - Vomiting
  - Diarrhea
  - Abdominal pain
  - Hypovolemia

- **Diagnosis**
  - History of ingestion
  - Clinical signs
  - Bloodwork
NSAIDs

- **Carprofen:**
  - GI signs: >4 mg/kg cats, >20 mg/kg dogs
  - Renal signs: >8 mg/kg cats, >40 mg/kg dogs
  - Neuro signs: dose unknown

- **Derramax:** In dogs
  - GI signs: >15 mg/kg
  - Renal: >30 mg/kg

- **Naproxen:** In dogs
  - GI signs: >10 mg/kg
  - Renal and neurologic: >50 mg/kg

- **Ibuprofen**
  - GI signs: >25 mg/kg cats, >50 mg/kg dogs
  - Renal: >100 mg/kg dogs
  - Neurologic: >400 mg/kg dogs
NSAIDs

Most severe GI signs occur when NSAIDs are combined with corticosteroids

Treatment:
- Emesis/gastric lavage
- Activated charcoal
- IVF diuresis X 72 hours
- GI protectants X 5-7 days
- Monitor CBC, chemistry, urine production

Acetaminophen

Metabolism
- 90% to sulfate & glucuronide (nontoxic)
- 5% excreted unchanged in urine
- 5% NAPQI
Acetaminophen

- NAPQI: a nontherapeutic metabolite
  - Alters chemical structure of proteins and lipids
  - Cellular damage
- Metabolized by binding with sulfhydryl groups of glutathione

NAPQI

- ROS
  - Binds to cellular macromolecules
    - Lipid peroxidation & direct cell injury

NAPQI

- Patients with liver disease
- Toxicity is more severe and at lower levels
- Also:
  - Liver
  - RBC
  - GI
  - CNS
Acetaminophen

- Clinical signs:
  - Depression
  - Weakness
  - Hyperventilation
  - Icterus
  - Methemoglobinemia
  - Facial/paw swelling
  - Cyanosis

Acetaminophen

- Cats are very sensitive. No dose is safe.
- Dogs:
  - Hepatotoxicity: 75-100 mg/kg
  - Methemoglobinemia: 200 mg/kg

Acetaminophen

- Treatment:
  - Emesis/gastric lavage
  - Activated charcoal
  - Serum: alb., ALT, AST, T. Bili.
  - Will rise in 24 hours, peak at 48-72 hrs
**N-acetylcystine**

- Loading dose: 140 mg/kg PO
- 70 mg/kg PO x 6 treatments

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**Acetaminophen**

- Vit. C:
  - 30 mg/kg PO/IV q 6-12 hours
- Cimetidine
  - 5-10 mg/kg PO/IV q 6-8 hrs
- SAMe
  - Canine: 40 mg/kg PO, then 20 mg/kg Po SID
  - Feline: 180 mg/kg po, 90 mg/kg po q 12-24 hrs

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**Acetaminophen**

- Symptomatic patients
  - O2 support
  - IVF therapy
  - GI protectants
SSRI
- Selective serotonin reuptake inhibitor
- Antidepressant

SSRI
- Serotonin
  - Biogenic amine
  - Produced from essential AA tryptophan
- Majority produced in CNS
- Small amt produced in platelets

SSRI
- Serotonin
  - Outside CNS
    - Platelet aggregation
    - Maintains vascular tone
    - GI motility
SSRI

- Serotonin
  - CNS:
    - Stored in pre-synaptic vesicles of serotoninergic neurons, pineal gland and catechoalminergic neurons

SSRI

- Serotonin
  - CNS: Released
    - Binds to serotonin-specific receptors on postsynaptic membrane
    - Binds to autoreceptors on the presynaptic membrane
    - Which act a neg feedback for serotonin release.

SSRI

- Serotonin
  - Binding to a selective serotonin transporter removes the serotonin
  - Metabolized in presynaptic cytosol by monoamine oxidase
SSRI

- Clinical signs
  - GI signs
  - CNS depression
  - CNS stimulation
  - Hypertension
  - Hypotension
  - Tachycardia
  - Tremors
  - Hyperthermia

SSRI

- Serotonin syndrome
  - Characterized by altered mental status, behavioral changes, altered muscle tone, altered neuromuscular activity, autonomic instability, hyperthermia and diarrhea.
  - Generally seen when multiple serotonergic agents are ingested
  - TCAs and MAOIs most commonly implicated

Retrospective evaluation of toxicosis from SSRI antidepressants, 2005-2010 (VCEC 2012): 674-681

SSRI

- Diagnosis
  - Based on history of ingestion
SSRI

- Treatment
  - Bloodwork
  - Decontamination
  - Activated charcoal
  - Acepromazine 0.02-0.03 mg/kg IV for agitation/hypertension

- Vasopressors for hypotension
- Ciprohepatidene 1.1 mg/kg PO or per rectum
- Antiseizure medication (midazolam, Levetiracetam, phenobarbital)
- Propanolol
- IVF do not hasten excretion

SSRI

- Metabolized in the liver
  - Hepatic disease may worsen prognosis
  - Exposure to medications that inhibit cytochrome P 450 (ketoconazole) may increase potential for toxicity

Conclusions

- Always consider pet mental status, concurrent conditions and toxin ingested prior to inducing emesis
- When dealing with toxicities consider medications pet may be taking
- In cases of ingestion of multiple drugs or if unfamiliar with drug call poison control

QUESTIONS??