What's Your Next Move?" – An Interactive Review of Cases from the ASPCA Animal Poison Control Center

> University of Illinois College of Veterinary Medicine Fall Conference

> > September 18, 2015

I

COLLEGE OF VETERINARY MEDICINE

Faculty

Michael Biehl, DVM, PhD, DABTClinical Professor of Toxicology, College of Veterinary Medicine

Tina Wismer, DVM, DABVT, DABT

Medical Director, ASPCA Animal

Poison Control Center (APCC)

COLLEGE OF VETERINARY MEDICIN

1

"What's Your Next Move?" – An Interactive Review of Cases from the ASPCA Animal Poison Control Center

Interesting and informative cases (both recorded phone calls and case histories) from the ASPCA Animal Poison Control Center will be presented and discussed in an interactive format. Participants will self-select diagnostic and treatment options followed by a group discussion regarding those choices.

I

Course Activities

- We will present case histories via Powerpoint presentations
- We will then use actual recorded calls from past APCC cases files.
- <u>Using I-Clickers</u>, you will be given the opportunity to self-select diagnostic and treatment options based on your experience and/or current knowledge.
- We will discuss the rationale for the various choices and additional toxicant information in a group format.

1

COLLEGE OF VETERINARY MEDICINE

APPC Case – Practice Question How many games will the Illini football team win this year? a) 1-3...."Bring back Beckman!!" b) 4-5....The "Cubit Era" is short-lived c) 6-7....Bowl bound d) 8-10...."I Believe" e) When does basketball start?/I don't care



True or False?

"If I don't know what the poison/antidote is, I can't treat the animal!" A) True B) False

FALSE!

"Treat the patient, not the poison"



Initial Contact

- You are at work and the phone rings
 - The caller says they have a dog that has been coughing for a few days, but this weekend the dog seems worse. Oh, by the way, she could have gotten into some rat poison a few days ago...
 - You request that the owner bring in the dog right away and find out what kind of rat poison the dog could have eaten.

Rodenticides

- Commonly encountered
- Accurate identification required
 - Each class unique
 - Clients must bring box/bait in to clinic to aid ID.
- Color and formulation not unique
- - Baits come in blocks, pellets and granules
 - Blue, green, red or tan

Physical Exam

- 8 year old F/S Shep. X 72# – QAR
- T= 101.8
- HR=98, no pulse deficits - m. membranes slightly pale, CRT < 2 s
- R=panting
 - lung sounds are uniformly harsh in all quadrants, no crackles or wheezes noted

Physical Exam

- Eyes lenticular sclerosis
- Teeth dental tartar moderate
- Abdomen dog seems painful and resists abdominal palpation by tensing

What do you want to do next?

- A) More history
- B) CBC, chem panel
- C) Radiographs
- D) Ultrasound
- E) MRI
- F) Recommend euthanasia

Additional History

- Coughing began about 3 days ago
- Dog has not wanted to eat in the past 2 days and today has even refused water.
- Rat poison was in basement and dog was found there about 5 days ago; unknown if any was ingested.
- Other dog in household is normal.

- Your assistant hands you a box of D-Con Mouse Prufe II. The active ingredient is brodifacoum 0.005%.
 - Anticoagulant rodenticide

Anticoagulants

- Inhibit vitamin K 1,2,3-epoxide reductase - Stops production of clotting factors
- Prevents vitamin K recycling
- Affected factors

pathways

II, VII, IX, and X
 extrinsic, intrinsic common





Back to our patient...

 Could anticoagulant ingestion account for the clinical signs in our dog?

 coughing, ADR

–A) yes

-B) no

What do you want to do next?

- A) radiographs
- B) coagulation panel
- C) ultrasound
- D) referral to the university
- E) give Vitamin K1
- F) thoracocentesis

Thoracic radiograph

• Does this look like rat poison?





Differentials?

- Neoplasia
- Neoplasia
- Neoplasia
- Fungal



Outcome

• Owner's elected euthanasia due to poor prognosis.

Active ingredient	2008	2009	2010	2011	2012	2013	2014
Chlorophacinone	60	55	45	86	61	98	53
Diphacinone	239	210	201	231	285	259	250
Warfarin	71	45	54	34	47	36	36
Brodifacoum	1415	1429	1426	1469	1657	1675	1442
Bromadiolone	2205	2175	2453	1874	1770	1640	1412
Difenacoum	0	2	9	11	14	8	6
Difethialone	379	502	695	613	492	367	213
Bromethalin	2220	1590	1249	1412	1541	1615	2112
Cholecalciferol	91	69	57	56	56	59	27
Zinc phosphide	234	237	264	202	219	207	192
Total	6914	6314	6453	5988	6142	5964	5743





Case

• Mimi

• Shih Tzu

• 6y old

• F/I



- 12#
- No previous problems

History

- Mimi has vomited a couple times in the past few days
- Today she seems lethargic and doesn't want to eat
- No known toxin ingestion

PE

- Depressed but responsive
- T=101F
- P=120
- R=40
- Gums pale
- Abdomen palpates normally

• What do you want to do next?

- A. Radiographs
- B. CBC, chem panel, UA
- C. Ultrasound
- D. Euthanasia

- Start with CBC, chem panel, UA

Blood work

- PCV = 14%
- BUN = 50 (high)
- Creat = 2.9 (high)
- Serum noted to be red

Urinalysis

• Red

- Positive for hemoglobin - No intact RBCs seen
- pH = 7
- Protein high

Differentials?

- Bladder/renal stones, Bladder/renal tumor, Cystitis, Pyometra
- Should see intact RBCs, not just hemolysisLymphsarcoma, hemangiosarcoma
- Can see hemolysis in some cases
- IMHA
- Heartworm
 - Caval syndrome
- Toxins
 - Zinc, anticoagulants, onions/garlic

Any more diagnostics?

- Coombs test, Zinc level - Turn around time 2-3 days
- Radiographs - Metallic density in stomach
- Zinc toxicosis!





How do we treat this dog?

- Blood transfusion
- Fluids
- Surgery or endoscopy



- Pennies minted since 1983 are 97.5% zinc and 2.5% copper
- Zinc – Anemia, kidney failure



Treatment

• Mimi received a transfusion - Pre-op PCV = 25



- IV fluids
- Surgical removal of pennies
- Do we chelate?
 - A. Yes
 - B. No
 - No, levels drop quickly once remove

Case

- Husky, 4y M/N
- Presents with "swollen eyes"





Case

- The dog has chocolate colored mucus membranes.
- When you draw blood it looks like the sample on the left.



- What is your diagnosis?



Acetaminophen

- Changes blood so it can't carry oxygen

 Methemoglobinemia

 - Gums and blood muddy brown in color
- Liver failure







Treatment

- Which of the following would you like to use to treat this dog?
 - A. Activated charcoal
 - B. N-Acetylcysteine
 - C. Cimetidine
 - D. Famotidine
 - E. Blood transfusion

N-Acetylcysteine promotes glutathione production by body to enhance NAPQI conjugation and elimination (see previous slide).

Case

- The dog recovers uneventfully and goes home within 36 hours.
- The dog represents with this about 72 hours later:
- Is this related to the acetaminophen?



Yes!! KCS can be observed in dogs subsequent to acetaminophen exposure.



- History of vomiting today and lethargic tonight
- PE is WNL
- What would you like to do?
 - A. Radiographs
 - B. Blood work
 - C. Ultrasound
 - D. Euthanasia

- BUN 52 (14 36)
- Creat 4.9 (0.6 2.4)
- All other values WNL
- Diagnosis?
 - A. Acute renal failure
 - B. Chronic renal failure
 - C. Can't tell from this information...

History

- The owner said she sprayed Mac yesterday with flea spray
- Do you think the flea spray is involved? *Probably not*
- What other questions do you want to ask the owner?

Additional History

- Mac's owner had a death in the family and brought home several plants from the funeral
- The owner has observed Mac chewing on some of the plants
- The owner is able to identify the plants from the internet

Plant #1

- What is this plant? – Peace Lily (*Spathiphyllum* sp.)
- Does it cause renal failure?

– No

- Insoluble calcium oxalates
- Drooling, oral irritation, vomiting
- Pharyngeal swelling (rare)





Plant #2

- What is this plant? - Cala Lily (*Zantedeschia* sp.)
- Does it cause renal failure?
 - No
 - Insoluble calcium oxalates



Plant #3

- What is this plant? - White lily (*Lilium* sp.)
- Does it cause renal failure?

– Yes

- Unknown mechanism



Treatment

- IV fluids; 2-3X maintenance fro 24-48 hrs
- Monitor urine output
- Monitor electrolytes
- Antiemetics as needed
- Prognosis?

Lily

- Cats
- Emergency!!
- Kidney failure observed within 18-24 hrs
- ANY exposure to a "true lily" (*Lilium* or *Hemorcallis* sp.) merits aggressive veterinary care.



The word lily may be misleading (can you identify the "true" lily?)



Convallaria (lily of the valley)

cardiotoxin



Spathiphyllum (peace lily) calcium oxalates; GI upset

Lilium longiflorum (Easter lily) Nephrosis in cats



Case

- The dog walker brings in Chance, a neutered male, 3 yr old Golden Retriever for ataxia and tremors.
- The dog walker found Chance this way 30 minutes ago.



Physical Exam

- Mild to moderately ataxic on all limbs
- Full body tremors which are worse in the hind legs
- Slight disorientation
- T = 103.7 F
- P = 140
- R = panting
- CRT < 2 s

What do you want to do first?

- A. Obtain more history
- B. Give diazepam
- C. Give methocarbamol
- D. Call owner for permission to treat
- E. Give atropine

All reasonable answers

• The dog walker found Chance in the kitchen tremoring. He was behind a baby gate and there was no noticeable vomiting or diarrhea.



Agents Causing Tremors/Seizures

- ➤ Ethylene glycol
- Tremorgenic mycotoxins
- ➢ Strychnine
- Metaldehyde
- > Aminopyridine
- ≻ Lead

- ≻ 5-Fluorouracil
- \succ Methylxanthines
- ≻ Nicotine
- \succ Amphetamines
- ➤ Cocaine
- \succ Antidepressants
- > Antihistamines
- ≻ Isoniazid

- You are able to get in touch with Chance's owner at work
 - Dog got into the garage this morning before work (about 6 hours ago)
 - Chance was in the garage for about 30 minutes
 - Trash was knocked over
 - Bottles and containers strewn around

Further questions for owner?

- What was in trash?
 - Spoiled chicken, wrappers, paper towels, etc.
- What type of containers/bottles?
 - Antifreeze
 - Lawn fertilizer
 - Wind shield washer fluid
 - owner is unsure how much, if any, of these were ingested

How do we determine what is causing the problem?

- A. CBC
- B. Chemistry panel
- C. Ethylene glycol test
- D. Urinalysis
- E. Ultrasound
- F. Magic 8 Ball



Ethylene Glycol Test

- Chance's test is positive. – Patient sample on left
 - Control on right





Any further testing required?

- BUN, creatinine
- help assess prognosis
- Blood gases
 - acidosis
- Calcium
 - hypocalcemia
- CBC
 - assess dehydration

Why is ethylene glycol so bad?

- Ethylene glycol
 - Parent compound has significant alcohol related effects (CNS depression, GI irritation)
 - Metabolites of EG have more serious effects:
 - Sever metabolic acidosis
 - Renal tubular injury
 - Hypocalcemia (formation of Ca oxalate crystals which ppt in kidney)



Ethylene Glycol - Treatment

- Ethanol
 - Best within first 6-8 hours; metabolized by ADH enzyme so can't produce toxic EG metabolites.
 - Inexpensive, readily available
 - Contributes to acidosis and CNS depression
- Fomepizole (4-methylpyrazole, Antizol-Vet)
 - Inhibits ADH enzyme so can't produce toxic EG metabolites. Do NOT give concurrently with Ethanol → Ethanol toxicosis results!!
 - Does not worsen acidosis or CNS depression
 - More expensive than ethanol
- IV fluids, calcium, bicarb

Ethylene Glycol

- Prognosis
 - Guarded, depends on degree of exposure, time until treatment and aggressiveness of therapy
 Peritoneal dialysis or kidney transplant
 - Treatment for residual renal injury may require long-term therapy

Back to Chance

- BUN = 120
- creat = 4.5
- Owner elects to treat with 4-MP even with poor prognosis
 - Chance unfortunately begins to seizure and owner elects euthanasia



Bromethalin

- Rodenticide primarily rats/mice, also some mole baits
 Neurotoxin NOT an anticoagulant!
 - Often contain 0.01% bromethalin; mole baits 0.025%
 0.75 oz place packs, 0.5 oz bars, pellets
- Real Kill[®], Assault[®], Vengeance[®], Sudden Death[®], Fastrac[®], TomCat[®]







Bromethalin Clinical Signs

- Acute/Convulsant Syndrome (doses at or above LD₅₀)
 - Signs appear 10 to 24 hrs post ingestion
 - Mortality rate ~100%
 - Agitation, depression, hyperesthesia, hind limb paresis, tremors, seizures, death
- Chronic/Paralytic Syndrome
 - Signs occur 1 to 5 days post exposure
 - · Ataxia, rear limb paresis, tremors, depression, recumbency, decerebrate posture (flexed forelimbs, rigid hindlimbs) and seizures terminally.

1

Bromethalin

- Treatment
 - Brain edema Corticosteroids, furosemide, mannitol
 - · Can try but effectiveness varies
 - Treat seizures symptomatically (diazepam,
 - phenobarbital)
 - Repeated doses of activated charcoal
 - Bromethalin undergoes enterohepatic recirculation • Watch for hypernatremia!! Fluids; monitor sodium levels
 - Lipid therapy; questionable effectiveness??
 - Supportive care

 - DO NOT give vitamin K!! This is NOT an anti-coagulant Prognosis - varies with severity of signs

1

I-Clicker Question – Bromethalin 1

Do you agree with the recommendation to not administer Activated Charcoal if you get bait back intact?

a) YES

b) NO

Maybe yes, maybe no!! No..... Small dog, hypernatremia risk Yes....are you sure some bromethalin did not leach off of bait before induced emesis?

COLLEGE OF VETERINARY MEDICINE							
MDAC Decontamination - Dog							
Time since exposure	Dose Ingested (mg/kg)	Action Needed					
< 4 hours	0.1 - 0.49	Emesis or one dose of charcoal					
> 4 hours	0.1 - 0.49	One dose of charcoal					
< 4 hours	0.5 - 0.75	Emesis and three doses of charcoal					
> 4 hours	0.5 - 0.75	Three doses of charcoal					
< 4 hours	> 0.75	Emesis and three doses of charcoal per					
		day for 48 hours					
> 4 hours	> 0.75	Three doses of charcoal per day for 48					
		hours					
		7					
		-8					



COLLEGE OF VETERINARY MEDICINE						
MD	MDAC Decontamination - Cat					
Time since exposure	Dose Ingested (mg/kg)	Action Needed				
< 4 hours	0.05 - 0.1	Emesis or one dose of charcoal				
> 4 hours	0.05 - 0.1	One dose of charcoal				
< 4 hours	0.1 - 0.3	Emesis and three doses of charcoal				
> 4 hours	0.1 - 0.3	Three doses of charcoal				
< 4 hours	> 0.3	Emesis and three doses of charcoal per day for 48 hours				
> 4 hours	> 0.3	Three doses of charcoal per day for 48 hours				
> 4 hours	> 0.3	Three doses of charcoal per day for 48 hours				
		<u>11</u>				



COLLEGE OF VETERINARY MEDICINE **Xylito** Sugar substitute Candies, gums, toothpastes, mouthwashes, baked goods

Treat at 0.1 g/kg or greater •

٠ •

- Check label for listing of sugar alcohols May say "Sugar alcohol 2.0 g" per serving (1 pc) •
- If in doubt, assume 0.3 gm xylitol / piece of gum
- Profound hypoglycemia in dogs
- Rapid rise in insulin levels
- Drop in blood glucose
- Overall depletion of ATP, hepatic cellular homeostasis impaired T

- Xylitol Clinical Signs
- ٠ Vomiting
- ٠ Depression, lethargy, weakness, ataxia
- Seizures
- Hypoglycemia generally •
 - Hyperglycemia in some cases "Symogi Syndrome"
 - Hypokalemia, hypophosphatemia possible
- Rapid onset 15 30 minutes
- Liver failure possible •
- Large ingestions (>1.3 gm/kg)
- Enzyme elevations by 12-24 hours
- If no hepatic effects by 3 days, probably Ok. •

1

Xylitol - Treatment

- Obtain baseline glucose, K, P, liver enzymes, total bilirubin, coagulation parameters
 - Continue to monitor BG q 1-2 hours for 12 hours
 - Others q 12 hours for 72 hours
- If hypoglycemic
- Dextrose bolus and CRI
- Small frequent meals
- Hypoglycemia may be prolonged •
- Potassium supplementation if <2.5 mmol/L
- May require 12 24 hours or longer

1

Xylitol treatment con't

- For large ingestions (>1g/kg)

 Same as previous except start dextrose immediately
 Liver protectants
 - SamE, Marin, Vitamin E
 Plasma / blood transfusions
- Prognosis

 - Good for uncomplicated hypoglycemia or mild liver enzyme elevation with prompt treatment
 Guarded to poor with severe elevation of liver enzymes, hyperbilirubinemia, hyperphosphatemia, coagulopathy

1



Amphetamines

- Many derivatives of amphetamines
- Prescription (obesity, ADHD, narcolepsy) - Ritalin®, Concerta® (methylphenidate)
 - Cylert ® (pemoline)
 - Adderall ®
 - "Fen-Phen" (fenfluramine and phentermine)

I

- Over the counter (decongestants)
 - Pseudoephedrine

Amphetamines

- Illicit
 - Amphetamine (speed, uppers, dex, bennies)
 - Methamphetamine (ice, crystal, crank, meth)
 - Designer amphetamines
 - 4-methylaminorex (ice, U4EUh)
 - 3,4-methylene-dioxymethamphetamine, MDMA (ecstasy, XTC, Adam, MDA)
 - 3,4-methylenedioxy-N-ethylamphetamine, MDEA (Eve)
 - methcathinone (cat)
 - Cocaine
 - Potential for more cardiovascular effects, esp. hypertension

1

COLLEGE OF VETERINARY MEDICINE

Amphetamines

- Exact mechanism of action unknown
 - Enhances release and decreases reuptake of catecholamines and serotonin
 - Directly stimulate alpha and beta adrenergic receptors, dopamine receptor agonists
- Low margin of safety
 - Dog (oral) LD50 amphetamine = 20–27 mg/kg
 - Dog (oral) LD50 methamphetamine = 9-11 mg/kg

1





APPC Case - Adderall
Adderall® is an amphetamine for ADHD. What drug is contraindicated in therapy?
a) Atropine b) Benzodiazapines (e.g. Diazepam) c) Methocarbamol d) Acepromazine
Benzodiazapines!! Worsens Agitation.

I

COLLEGE OF VETERINARY MEDICINE APPC Case - Adderall Adderall is a weak base. Do you want to: a) Acidify , or b) Alkalinize the urine? Acidify urine to maintain BH+ preventing systemic reabsorption from urine and enhancing excretion. Watch acid/base status!! $BH^+ \leftarrow \rightarrow B + H^+$

Amphetamines – Treatment • Emesis? Rapidly absorbed • *Phenothiazines*

- · Gastric lavage
- Activated charcoal - Multiple doses for extended release
- products • IV fluids, control
- hyperthermia
- Avoid benzodiazepines!
- Will increase agitation
- Urinary acidification
- chlorpromazine, acepromazine As high as 1 mg/kg

"cool them down"

- Cyprohepatadine
- serotonin antagonist Beta-blocker for
- tachyarrhythmias
- propranolol,
- metoprolol

Amphetamines

- Rapid absorption
 - Readily penetrates blood-brain barrier
- · Hepatic metabolism, renally excreted - Ion trapped - weak base BH+, so more excreted in acidic urine
 - Half life:
 - acid urine: 7 hours
 - alkaline urine: 34 hours
 - Consider acid-base status of animal before acidifying urine!!

1

Serotonergic Drugs

- Selective serotonin reuptake inhibitors (SSRIs) - Sertraline (Zoloft), Fluoxetine (Prozac), Paroxetine (Paxil), Fluvoxamine (Luvox; CATS SEEK IT OUT !!)
 - Venlafaxine (Effexor; also NE uptake inhibitor; esp. problem in cats)
- Monoamine oxidase inhibitors (MAOIs)
- Tricyclic antidepressants (TCAs)
 - Amitriptyline, Clomipramine, Doxepin, Imipramine, Nortriptyline
 - More CV effects; enterohepatic recirculation \rightarrow long half life
- Atypical antidepressants

Decontamination

- Emesis
 - If asymptomatic and no other contraindications
- Activated charcoal
 - Most medications bind well (except lithium)
 - Repeat if TCAs or enterohepatic recirculation

1





Lipid Therapy

- Lipid emulsion is commonly used as a fat component for parenteral nutrition
- Promising new treatment for toxicosis due to lipophilic agents.
- Usage based on human research investigating bupivacaine
- Mechanism for lipid rescue - Possible "lipid sink"



COLLEGE OF VETERINARY MEDICINE

1

Lipid Therapy

- While more studies are needed, lipid therapy is very exciting for management of toxicosis due to lipid soluble (fat-soluble) agents.
- Can hasten recovery time
 - Reduced time for intensive care
 - Option that may save pet from being euthanized
 Less \$\$ cost
- Baclofen, avermectins, serotonergic agonists, calcium channel blockers, bromethalin(??)

1

COLLEGE OF VETERINARY MEDICINE

Dosing Protocol

- 20% lipid solution
- Initial bolus at 1.5 ml/kg (over 1 minute if cardiac arrest, slower otherwise) then 0.25 ml/kg/min for 30-60 min
- Repeat dose every 4-6 hours if needed
- Check for hyperlipemia before repeating dose

 Re-dose only if serum is clear

APCC Cases - Permethrins

For permethrin intoxications in cats, *ideally* _______ is used to counter the *seizures* and _______ for treating *tremors*.

1

- a) IV methocarbamol; IV valium
- b) oral valium; IV methocarbamol
- c) IV valium; IV methocarbamol
- d) IV valium; IV atropine









Pharmacokinetics

- NSAIDs are weak acids
- Well absorbed following oral administration - Bioavailability ranges from 60-100%
- ٠ Low serum albumin - Higher concentrations of active drug
 - Increased adverse reactions and toxicity
- NSAIDs are highly protein bound
 - Can displace or be displaced by other highly protein bound drugs; may need to adjust dosage
- · Metabolized primarily by the liver - Glucuronidation
 - Cats are more sensitive to NSAID toxicosis

1

Pharmacokinetics

- · Age and health may also lead to increased sensitivity
 - Geriatric patients may require smaller doses because clearance of NSAIDs is decreased
 - Young animals have a higher volume of distribution of NSAIDs

 - Pre-existing renal, cardiovascular, or hepatic disease may be more likely to predispose to adverse reactions or toxicities

1

 Patients who experience hypotension or receive other nephroactive or nephrotoxic drugs may be more prone to develop nephropathy

APPC Case - NSAIDs

What is the primary adverse clinical sign observed with lower doses of NSAIDs? a) Methemoglobinemia b) Acute renal failure c) Hepatitis

d) GI irritation/ulceration

e) Pancreatitis *GI irritation/ulceration*

Higher Doses? *Renal – constriction of afferent arteriole*

I

COLLEGE OF VETERINARY MEDICINE

APPC Case - NSAIDs

What is the primary therapeutic agent used to treat the GI signs due to NSAIDs?

- a) Sucralfate
- b) Misoprostol
- c) An H2-receptor antagonist (e.g. Famotidine)
- d) Proton pump inhibitors
- e) All of the above

All of the Above

I



