Rodenticide Toxicity:
Lunch and Learn

Ed Park, DVM, DACVECC
Fresno Veterinary Specialty and Emergency Center
April 24, 2013
Rodenticide Toxicity

• Most common rodenticide toxins:
  A) Anti-coagulant- warfarin derivatives
  B) Bromethalin
  C) Cholecalciferol

-Rodenticide intoxication is common in dogs
-Rare in cats
-Identification is paramount to treatment
Rodenticide Toxicity

• Questions to ask upon presentation:
  A) Rat poison on the property?
  B) Do you have the packaging?
  C) Any chance of rodenticide ingestion?
GI Decontamination

1) Emesis Induction - up to 4 hours
   Dogs
   a) Apomorphine - 0.04-0.08mg/kg IV
   b) Hydrogen Peroxide - 1-5ml/kg PO
   Cats
   a) Xylazine

2) Gastric Lavage - controversial

3) Activated Charcoal
Anticoagulant Rodenticides

Examples

- d-CON
- Notrac®
Anticoagulant Rodenticides

-Mechanism of Action:
Inhibition of vitamin K epoxide reductase

-Factors affected: II, VII, IX, X
# Anti-coagulant Rodenticides

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>CLASSIFICATION</th>
<th>TRADE NAMES</th>
<th>SUPPLIER</th>
<th>PRESENTATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; generation anticoagulant</td>
<td>Various</td>
<td>Generic</td>
<td>Meal, Water</td>
</tr>
<tr>
<td>Pindone</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; generation anticoagulant</td>
<td>Pival&lt;sup&gt;TM&lt;/sup&gt;, Pivalyn&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>Generic, Generic</td>
<td>Meal, Water</td>
</tr>
<tr>
<td>Diphacinone</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; generation anticoagulant</td>
<td>Ramik&lt;sup&gt;TM&lt;/sup&gt;, Rampage&lt;sup&gt;TM&lt;/sup&gt;, Tomcat&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>Neogen, Liphatech</td>
<td>Blocks, Blocks, Liquid</td>
</tr>
<tr>
<td>Chlorophacinone</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; generation anticoagulant</td>
<td>Rozol&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>Liphatech</td>
<td>Pellets</td>
</tr>
<tr>
<td>Brodifacoum</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; generation anticoagulant</td>
<td>Havoc&lt;sup&gt;TM&lt;/sup&gt;, Jaguar&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>Neogen, Motomco</td>
<td>Blocks &amp; Pellets, Blocks</td>
</tr>
<tr>
<td>Bromadiolone</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; generation anticoagulant</td>
<td>Boothill&lt;sup&gt;TM&lt;/sup&gt;, Hawk&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>Liphatech, Motomco</td>
<td>Blocks, Meal &amp; Blocks</td>
</tr>
<tr>
<td>Difethialone</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; generation anticoagulant</td>
<td>Hombre&lt;sup&gt;TM&lt;/sup&gt;, Fast Draw&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>Liphatech, Liphatech</td>
<td>Blocks, Soft bait</td>
</tr>
</tbody>
</table>
Anti-coagulant Rodenticides

-Acute Management
1) Emesis induction within 4 hours
-Contraindications: seizures, severe depression
2) Activated Charcoal
-Sorbitol vs Non-sorbitol?
-Sorbitol- GI free water loss (hypernatremia)
3) Obtain PT with ingestion > 48 hours
Anti-coagulant Rodenticides

• Pachtinger Study (JVECCS 2008)

**Conclusions:** The incidence of prolonged PT is low in dogs receiving GI decontamination within 6 hours of anticoagulant rodenticide ingestion. Delaying vitamin K therapy until a PT has been assessed 48–72 hours after initial exposure appears to be safe and sensitive in dogs following anticoagulant rodenticide ingestion.
Evaluation

A) Coagulation Profile
   - PT prolongation before aPTT prolongation
   - 1/2 life of Factor VII is 6.2 hours
   - Clinical bleeding – begins once depletion of Factors II, IX, X occur (avg 3-5 days)
   - 1/2 life of Factor II is 41 hours

B) CBC, Chemistry Profile
Treatment- Stable Cases

-If PT is prolonged 48 hours post-exposure:
  Vitamin K1 (activated) for 4 weeks for 2’nd generation anti-coagulants
- Dose: 2.5mg/kg PO BID
- Re-check PT 48 hours following last dose
- If PT prolonged, additional Vitamin K for 1-2 months
Treatment: Unstable Cases

What constitutes an unstable case?

-Evidence of clinical bleeding
1) Documentation of toxin exposure
2) Prolongation of coagulation profile

Diff Dx:
1) Thrombocytopenia/Thrombocytopathia
2) DIC
3) Congenital Coagulopathy
4) Hepatic Failure
Definitive Dx

1) UC Davis Panel (utilizes spectrophotometry)
   Problem: return time is ~ 1 week

2) PIVKA? (3-fold increase)
   -Not specific; with elevations occurring with:
     a) Liver Disease
     b) Malabsorption / Maldigestion syndrome
Treatment- Symptomatic Patients

1) Correction of coagulopathy
   a) FFP (Fresh Frozen Plasma): 10-20ml/kg
   b) FWB (Fresh Whole Blood): 20mg/kg
   c) FP (Frozen Plasma): 10-20ml/kg

2) Vitamin K1: oral is better, SQ alternative

3) Oxygen Therapy

4) +/- Thoracocentesis or Pericardiocentesis
Prognosis: Anti-coagulant

- Prognosis is EXCELLENT
- ...even with clinically bleeding cases with aggressive tx
- Cost Factor: Clinical vs Non-Clinical
Cholecalciferol
Pathophysiology (cholecalciferol)

-Vitamin D3 $\rightarrow$ 25-hydroxycalciferol (via hepatic metabolism) $\rightarrow$ 1, 25-(OH)$_2$ cholecalciferol (via renal metabolism)

-1,25 dihydroxycholecalciferol:
  a) Increase Ca$^{2+}$ GI absorption
  b) Increase Ca$^{2+}$ bone resorption
Clinical Signs

-C/S seen are referable for hypercalcemia
-4 to 36 hours for C/S to occur:
  a) PU/PD
  b) Lethargy
  c) Anorexia
  d) Vomiting
  e) Cardiac Arrhythmias

-Primary effects occur due to AKI and cardiac arrhythmias
Bloodwork (Cholecalciferol)

A) Hypercalcemia
   Elevated Total Calcium
   Elevated iCa2+ (more accurate)
B) Hyperphosphatemia
C) +/- Azotemia with dilute USG
Hypercalcemia- Diff Dx

A) Primary Hyperparathyroidism
B) Hypoadrenocorticism
C) Renal Failure (secondary hyperparathyroidism)
D) Osteolytic Lesions
E) Neoplasia – LSA, Anal Sac ACA, Myeloma
F) Granulamatous Disease (fungal, etc)
Treatment (hypercalcemia)

A) IV Fluid Diuresis (0.9% NaCl)
B) Furosemide (after euvoolemia established)
C) Glucocorticoids
D) Calcitonin (salmon-based)
E) Pamidronate (Bisphosphonate)

-may need to repeat in 4 days
Prognosis (Cholecalciferol)

- None to mild azotemia $\rightarrow$ Fair to Good
- Hypercalcemia / AKI development $\rightarrow$ Poor
- Long-term therapy $\rightarrow$ tapering of both Prednisone and Furosemide over 4-6 wks
  - If needed, Lower Ca2+ diets (i.e. Hills T/D)
  - Close monitoring of iCa2+ and renal values
Bromethalin

Examples
Pathophysiology (Bromethalin)

- Uncoupling of oxidative phosphorylation
  - ATP depletion in the brain
  - Decrease in Na/ATP pumps in neuronal cells
  - Accumulation of intracellular Na+
  - Cell swelling resulting in increased ICP and cerebral edema
Clinical Signs (Bromethalin)

Neurologic symptoms predominate
1) Severe muscle tremors
2) Hyperexcitability
3) Seizures
4) Hyperthermia
5) Ataxia
6) Paresis/Paralysis

- High dose exposure (4.7mg/kg dogs, 1.8mg/kg cats) → C/S within 24 hours
- Low dose exposure → C/S within 24-72 hours
Treatment (Bromethalin)

-Acute Ingestion → standard decontamination (emesis- if no tremors/seizures, activated charcoal, +/- gastric lavage)
-Enterohepatic re-circulation (repeated doses of Activated charcoal advised q 6-8 hours for 48h)
Neurologic Complications (Bromethalin)

Vital to improve:

A) CPP → Cerebral Perfusion Pressure
   CPP = MAP – ICP
   MAP (BP) = CO X SVR

B) DO2 → Oxygen Delivery
   DO2 = CO X CaO2
   CaO2 = 1.34 X Hb X SaO2 + (0.003 X PaO2)
Neurologic Complications (Bromethalin)

Treatment:
A) IV Fluid therapy (to maintain BP)
B) O2 Supplementation (to improve DO2)
C) Methocarbamaol- up to 220mg/kg/day
D) Diazepam (for seizure control)
E) Mannitol (to reduce cerebral edema)
F) +/- Phenobarbital
Prognosis (Bromethalin)

- Poor prognosis with severe symptoms
  > 5mg/kg → no reports of survival
Misc Rodenticide Toxins

A) Zinc Phosphide
-Phosphine gas $\rightarrow$ Reactive Oxygen Species
-C/S: Vomiting, Lethargy, Tachypnea, Neurologic Signs, Rotting fish odor
-Tx: supportive care/decontamination

B) Strychnine
-Prevents uptake of glycine at Renshaw cells of CNS
-C/S: Convulsions, extensor rigidity, death
-Tx: Decontamination, Muscle Relaxation, Anti-convulsants
The End

Any Questions?