Rodenticides

The old, the new, and the ugly

Coag Lab CE 8-20-2015

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The Old – Warfarin

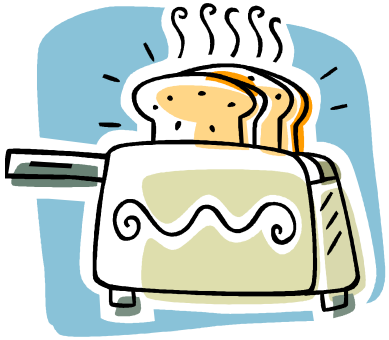
- Discovered in the 1940s
- First generation anticoagulant introduced in 1948
- Sold as Coumadin to prevent thrombosis in human medicine
- 15.5 hour half life
  - Requires multiple feeding to kill rodents
  - Many rodents have developed resistance
- LD_{50} for 20 pound dog – 3.6kg
  - ~8 pounds of bait

The Old – 1st Gen LAAC

- Indandiones
  - Diphacone and Chlorophacinone
- 1st gen anticoagulants developed after warfarin
- Half life unknown but longer than warfarin
  - Only one feeding needed to kill rodents
- LD_{50} for 20 pound dog – 540g
  - ~1 pound of bait

The New – 2ng Gen LAAC

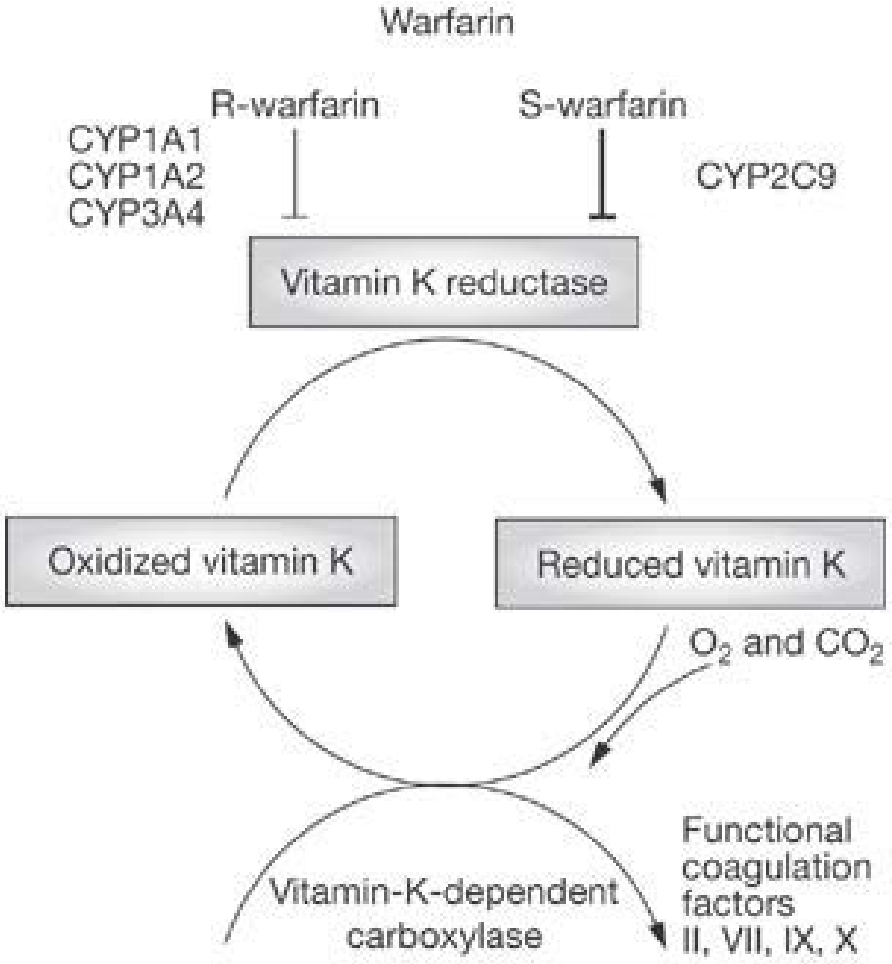
- Brodifacoum, bromadiolone, difethialone
- Much longer lasting
- Half life of 6 days in plasma, 180 days in the liver
- LD_{50} for 20 pound dog
  - Brodifacoum – 36g
  - Bromadiolone – 90g
  - Difethialone – 1.5kg



LAAC – How They Work

- Clinically significant dose prevents formation of functional factors II, VII, IX, and X
- Factor VII has the shortest half life ~6 hours
  - Factor II – 65 hours
  - Factor IX – 45 hours
  - Factor X – 40 hours
- PT becomes prolonged after 32-48 hours
- aPTT becomes prolonged after PT, both long by the time bleeding starts
- TCT, Fibrinogen, FDP, Platelet count all remain normal
  - Unless affected by significant bleeding
- Patients may develop anemia, cavity bleeds, joint bleeds, GI bleeding, hematomas

LAAC -How they Work



http://www.nature.com/nrclinonc/journal/v6/n3/fig_tab/ncponc1303_F4.html

LAAC Treatment

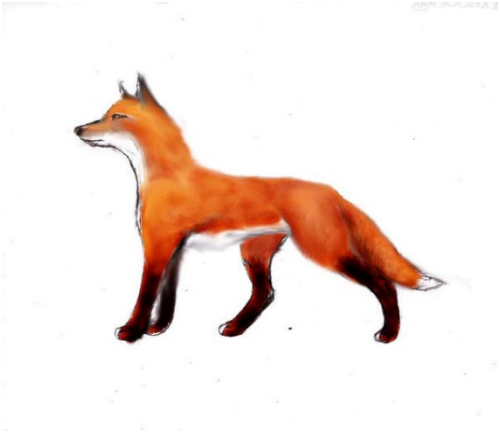
- Within 4 hours – induce vomiting, activated charcoal
- Vitamin K1
  - Initial dose 2.2 mg/kg SQ
  - 1.1 mg/kg SQ every 12 hours till bleeding stops
  - Oral Vit K 1.1 mg/kg twice a day 1-6 weeks
  - Do not use Vitamin K3
  - Do not give IV or IM
- Transfusion to control life threatening bleeding
  - FFP, FP, cryosupernatant to replace factors
  - FWB or pRBC to treat anemia
  - Do not use cryoppt
  - pRBC alone will not replace factors

LAAC Overview

Name	Type
Warfarin	1st gen
Diphacinone	1st gen
Chlorophacinone	1st gen
Brodifacoum	2nd gen
Bromadiolone	2nd gen
Difethialone	2nd gen

LAAC Problems

- Accidental poisonings of children, pets
- Bioaccumulation
  - ~50% of all NYS raptors test positive for LAAC
  - Most felids and foxes in CA test positive



New EPA Regulations

- Consumers
  - Remove second generation products, some non-LAAC OK
  - Products must be in bait stations, no loose pellets, bait refills OK
  - No more than 1lb bait per package
- Commercial
  - 2nd generation still available
  - Marketed for bait stations
  - >4lbs for 1 gen
  - 8-16lbs for 2nd gen
- Bait Stations
  - Tier 1 – indoor/outdoor, child/dog resistant, weather resistant
  - Tier 2 – Indoor only, Child/dog resistant
  - Tier 3 – Indoor only, Child resistant

EPA Regulations - consumer

Name	Type
Warfarin	1st gen
Diphacinone	1st gen
Chlorophacinone	1st gen
~~Brodifacoum~~	~~2nd gen~~
~~Bromadiolone~~	~~2nd gen~~
~~Difethialone~~	~~2nd gen~~
Bromethalin	Not a LAAC
Cholecalciferol	Not a LAAC

The Ugly - Bromethalin

- Inhibits ATP production in myelin cells
- Plasma half life is 6 days
  - Relay poisoning possible
- LD_{50} for 20 pound dog – 180g
  - Cats more sensitive – 45g

- High dose causes rapid increase in intracranial pressure
- Lower dose causes progressive demyelination
- Clinical signs within 24 hours
- **Indistinguishable from anticoagulant bait!**
  - Diagnosis from clinical signs, bait analysis, post mortem lesions

The Ugly - Cholecalciferol

- Vitamin D3
- Required for health
  - Calcium absorption and regulation
- High doses cause significant increase in plasma calcium and phosphorus levels which causes mineralization of the kidney
- LD_{50} for a 20 pound dog – 117g
  - Clinical signs can occur with as little as 24g
- Changes to blood chemistry within 12 hours
- Clinical signs 8-24 hours after exposure
- **Indistinguishable from anticoagulant baits!**
  - Diagnosis from serum calcium and phosphorus levels

The Very Ugly – Zinc Phosphide

- Reacts with stomach acid to form phosphine gas
- Prevents aerobic respiration causing tissue hypoxia
- LD_{50} for 20 pound dog – 3.6g to 36g depending on bait strength
- Clinical signs within 15 min
- Many products contain an emetic

  - May save patient, but puts owner and vet staff at risk!
  - Gas smells of acetylene, garlic or spoiled fish
  - Ventilate!
  - 4 clinics evacuated between 2006 and 2011
- Baits are grey-black powder sold pelleted or mixed with grain
  - Available to consumers as gopher bait

So What tests do we run?

- Coagulation testing
  - Coag Panel – add on FVII if PT/aPTT long, TCT normal
  - Factors VII, VIII, IX, X – Low VII, IX, and X, normal VIII - pretty definitive
  - Fairly inexpensive (can run as little as PT and FVII is money tight)
  - Only ante mortem citrated plasma
- Toxicology testing
  - Rodenticide anticoagulant screen on blood, urine, liver, stomach contents, feed
    - Brodifacoum, Bromadialone, Chlorophacinone, Dicoumarol, Difethialone, Difenacoum, Diphacinone, Flocoumafen, Warfarin
  - Postmortem sample from liver OK
  - Expensive - $165.50
  - Can send out samples for Bromethalin and Cholecalciferol

Vitamin K deficient but not poison?

- Rodenticide exposure not the only cause of Vitamin K deficient coagulopathy
- Biliary obstruction, intrahepatic cholestasis, chronic oral antibiotic administration, infiltrative bowel disease
- Hereditary deficiency of Vitamin K epoxide reductase or carboxylase enzymes
  - Humans, cats, sheep, Labrador retrievers
  - Recessive trait
  - RARE!

Questions?

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