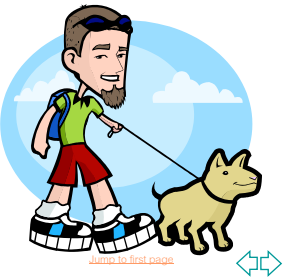
Rodenticides



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Introduction

A.Sources

1.Pastes & Pellets & Concentrates for mixing with water

2.Tracking powders

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B. Exposure

1. Anticoagulant rodenticides
2. Cholecalciferol based rodenticides
3. Zinc or aluminum phosphide
4. Strychnine based rodenticides

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B.Exposure

1.Recommended safety precautions are often ignored

2.Homed and businesses may rely on heavy use of rodenticides rather than fallowing good rodent control practices

3.Malicious poisoning

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Anticoagulants

A. Chemical Structure

1.Derivatives of 4-hydroxycoumarin or indane 1,3-dione

a. coumarin derivatives are warfarin, brodifacoum, bromadiolone & difenacoum

b. indanedione derivatives are pindone, chlorphacinone & diphacinone

c. Brodifacoum is used most frequently

d. Because of the warfarin-resistant rodents,warfarin,once uses commonly is now very little.

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B.Sources

The concentration of toxicant in baits ranges from 0.02-1.0%

C.Exposure

1. .have access to baits

2. Secondary toxicosis

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D.Toxicokinetics

1. Absorption is high (90%), and plasma peak within 12 hrs.

2. Distribution is prolong by strong binding to plasma proteins

3. Metabolism & excretion：MFOs form inactive metabolites, which are excreted in urine.

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E. Mechanism of toxicologic damage

Competitively inhibit vitamin K epoxide reductase.Clotting factors are dependent on reduced vitamin K.

F.Toxicity

1.Ruminant are less susceptibility than simple stomach

2.Drugs that displace anticoagulants from plasma binding sites may make more free toxicant

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G.Diagnosis

1.Clincal signs

a. SC.hematoma, epistaxis, gingival hemorrhage, dark tarry stools and hematemesis.

.1. Capillary hemorrhage

.2. Anemia, weakness, ataxia and dyspnea

.3. Heart rate is irregular

b. Hemorrhage

.1. Sudden internal hemorrhage

.2. In CNS

.3. Placental

.4. Articular

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2.Laboratory diagnosis

a.Hematology

.1. Activated coagulation time

.2. Activated prothrombin time

.3. Activated partial thromboplastin time

b.Radiography

c.Thoracentesis

d. Chemical analysis

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H. Treatment

1.Detoxification：within 8 hrs.

2. Supportive therapy

a. Transfusion（10-20 ml/kg）

b. be kept warm

c. unnecessary manipulation should be avoid

d.Thoracentesis

3. Antidotal：Phytonadione（vitamin K1）

a. Dog & cat：2-5 mg/kg PO fallowed by a fatty meal

3-5 mg/kg IM or SC

administrated daily at least 21-30 days

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b. Pigs：2-5 mg/kg IM or SC

c. Horses：not exceed 2 mg/kg

d.Ruminant：0.5-1.5 mg/kg SC or IM

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Cholecalciferal（vitamin D_3）

A.Chemical Structure：sterol structure is activated by irradiation of 7-dehydrocholesterol

B.Sources

1.Baits：concentrated of toxicant is 0.075%

2.Vitamin supplements

3. Feed additives

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C.Exposure

1. Careless use of rodent place packs

2. Excessive cholecalciferol or ergocalciferol（vitamin D_2）in feed.

3. Excessive use as a growth promoter in large-breed dogs.

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D.Toxicokinetics

1. Absorption：rapid & complete in small intestine

2. Distribution：carried by the plasma to liver & kidney

3. Metabolism：is metabolized in liver & converted to active form in the kidney

4. Excretion：are excreted primarily via bile and in the feces

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E.Mechanism of damage

1. Promotes calcium retention

   a. increasing the absorption

   b. promote osteoclastic resorption of bone

   c. increasing calcium reabsorption in kidney

2. Effect of vitamin D_3 overdosage

   a. Hypercalcemia induced conduction dysfunction in heart

   b. abnormal tissue mineralization

   c. cellular degeneration & necrosis

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F. Diagnosis

1. Clinical sign：often develop 12-36 hrs after consumption

a. depression, anorexia, vomiting, polydipsia, polyuria, diarrhea

b. renal failure

c. Heart sounds are slowed and prominent

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2. Laboratory

a. serum calcium increase

b. serum phosphorus increase

c. BUN & creatinine increase

d. urine specific gravity increase

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G. Treatment

1. Detoxification：within 3 hrs.

a. Emesis or gastric lavage

b. Activated charcoal fallowed with osmotic cathartic

c. Continuted administration of charcoal（0.5-1.0 g/kg tid.）for 1-2 days

2. Supportive treatment

a. Fluid therapy with normal saline & furosemide（5 mg/kg fallowed by 3 mg/kg tid.）

b. Corticosteroid administration（prednisone 2 mg/kg tid.）

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Strychnine

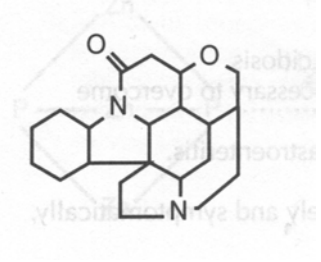
A. Chemical

1. Structure：indole alkaloid

2. Characteristics

a. relatively stable

b. Bitter



B.Source

1. Approved to bait gophers & ground squirrels（ Less than or equal to 0.5%）

2. Marketed as treated seeds or pellets

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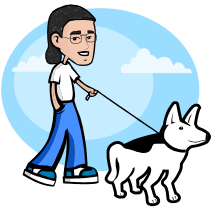
C.Exposure

1. Malicious poison for dogs
2. Careless use of baits
3. Secondary toxicosis



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D.Kinetics

1. Absorption：rapid from GI & respiratory mm.
2. Distribution：reach the CNS, liver, kidney
3. Metabolism：metabolized to strychnine-N-oxide by MFOs
4. Excretion：in urine（acidic urine enhances excretion）

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E.Mechanism：**antagonizes the inhibitory neurotransamitter glycine**

- **competitive & reversible**
- **major site of action**：**reflex arc in the spinal cord and medulla**

Keep The Dog

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F.Toxicity

1. **Dogs are more susceptible than cat**
2. **Large domestic animals are very sensitive**
3. **Poultry are relatively resistant**

Keep The Dog

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G.Diagnosis

1.Clinical signs

- Premonitory signs：nervousness, restlessness, muscle tremors & muscle tics in response to noise or sudden bright light
- Acute：
  - .1.explosive onset of tonic to tetanic seizures
  - .2.extreme sensitivwe to external stimuli
  - .3.vomiting is rare
- Advance sign：continuous tetanic seizures with marked rigidity, body temp. may be elevated, conscious, myoglobinuria

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2.Laboratory

- Acidosis
- elevated creatinine phosphokinase
- Myoglobinuria

Keep The Dog

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H.Treatment & prognosis

1.Detoxification

-Dogs in seizures must be relaxed and sedated before initiating detoxification therapy

- Gastric lavage in an anesthetized animal
- Gastric lavage should be followed by the administration of activated charcoal 2 g/kg and a saline carthartic
- Fluid diuresis
- acidified urine with ammonium chloride

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2.Supportive

- relaxed ---> prevent asphyxia
- Muscle relaxants
  - a. Glyceryl guaiacolate 110 mg/kg
  - b. Methocarbamol 150 mg/kg initially followed by 90 mg/kg
- Artificial respiration
- maintained in warm, quiet environment

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Phosphides of Zinc, Aluminum or Calcium

A. Characteristics

a. Calcium, aluminum, and zinc phosphides are brownish-red, gray to yellow, or dark gray crystals respectively

b. unstable in acidic or moist environments (decompose rapidly in stomach acids to form phosphine (PH_3)

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B. Sources

1. Rodenticides
2. Grain fumigants

C.Exposure

1. Ingestion of rodent baits or malicious baiting of dogs
2. Phosphine gas

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D. Toxicokinetics

1. Absorption：rapidly absorbed across mucous membrane

2. Metabolism & excretion：Phosphine is labile other are unknowns

E.Mechanism：respiratory & GI irritation & inhibit cytochrome C oxidase

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F.Toxicity

1.Acute toxicity：lethal dosage to most animals is between 20-50 mg/kg

2.Subacute & chronic toxicity are not described

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G.Diagnosis

1.Clinical sign：acute onset occurring within 0.5-4 hrs.

- Vomiting
- Depression , tremors, and weakness progressing to recumbency
- Hyperesthesia, seizures and running
- Salivation
- Colic（horse）,bloat（cattle）

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2.Laboratory

a.Hematology & clinical chemistry

- Both hyperphosphatemia & hypophospatemia
- Hypoglycemia & hypocalcemia
- Acidosis

3.Lesion

a.Stomach contents --> acetylene or “dead fish” odor

b.Pulmonary congestion & edema

c.myocardial degeneration, a pale yellow liver, fatty change & degeneration in the liver & kidneys

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H.Treatment

1.Detoxification：activated charcoal

2.Supportive therapy

a.Fluid with carbonate

b.Administration of oxygen

c.Demulcent & protectants

d.monitor serum calcium

e.Liver & kidney degeneration

Keep The Dog

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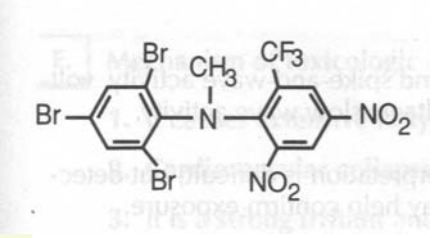
Bromethalin

A.Characteristics：pale yellow crystalline material, insoluble in water and stable at room temperature



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B.Source：

- alternative rodenticide to use against warfarin-resistant rat & mice

- package in place packs with bromethalin 0.01%

C.Exposure：inadvertent consumption, malicious poisoning

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D.Kinetics

1.Absorption：rapidly absorbed form GI

2.Metabolism：MFOs demethylate bromethalin to least toxic compounds

3.Excretion：primarily via the bile

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E.Mechanism of toxicity

1.uncouples oxidative phosphorylation

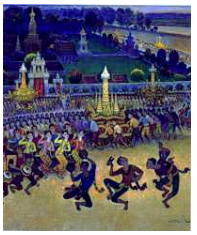
a. loss of sodium-potassium ATPase

b. intracellular edema

c. cell swelling

d. cell degeneration

2.cerebral lipid peroxidation



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F.Toxicity

1.Acute toxicity

TABLE 22-4. Acute Toxicity Values for Bromethalin

Species	Oral LD_{50}
Cats	1.8 mg/kg
Rats	2.0 mg/kg
Dogs	4.7 mg/kg
Rabbits	13 mg/kg
Guinea pigs	1000 mg/kg

2.Chronic toxicity：Prolonged exposure of rats to 10-20 ppm. dietary bromethalin

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G.Diagnosis

1.Clinical sign：dose-dependent

a.Acute signs：muscle tremors, hyperexcitability, paddling, hyperesthesia & fever

b.Subacute signs：posterior paresis, ascending ataxia, reduced conscious proprioception, loss of reflexes, depression & muscle tremors.

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2.Laboratory

a.EKG：abnoemal pattern of high voltage-slow wave

b. cerebrospinal fluid pressure is increased

3.Lesion：cerebral edema

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H.Treatment

1.Detoxification therapy

a.Emetics

b.Activated charcoal & saline carthartic

2.Supportive therapy

a.Mannitol（250 mg/kg every 6 hrs）

b.Dexamethazone（2 mg/kg every 6 hrs）

c.Fluid balance should be maintained with oral fluids

d.Seizures control with diazepam or phenobarbital