

Problem Based Approach to CNS Toxicities

Excitation or Seizures

Kathy Parton, IVABS



CNS

SEIZURES, EXCITATION

Differential diagnoses:

- Sodium fluoroacetate Compound 1080
- Metaldehyde
- Lead (Mixed CNS effects)
- Pyrethrins & Pyrethroids (mixed CNS)
- Ryegrass staggers

CNS

SEIZURES, EXCITATION

Differential diagnoses:

- Salt poisoning (water deprivation/Na)
- Chocolate (Mixed CNS effects)
- Organochlorine insecticides (DDT)
- Strychnine
- Herbicides: MCPA and 2,4-D

CNS Excitation Toxicities

1080 (sodium monofluoroacetate)

Sources of 1080:

Pesticide to control possums and other pests

- ∞ Pelleted bait or
- ∞ Impregnated carrots
- ∞ dyed black or green
- ∞ poisoned carcasses



CNS Excitation Toxicities

1080 TOXICITY

TOXICITY:

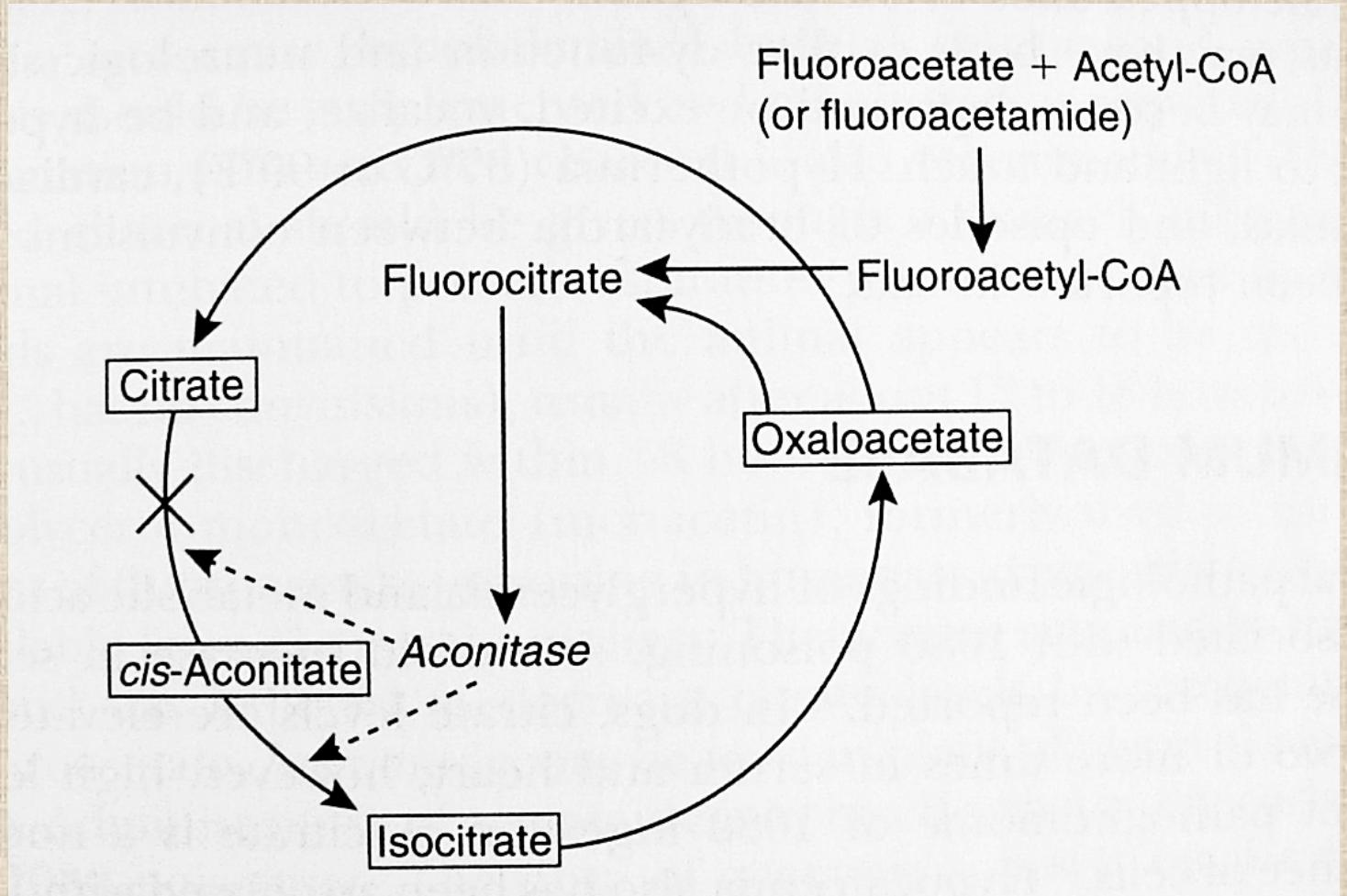
- Extremely toxic
- < 1 mg/kg oral lethal dose for:
- cats, dogs, rabbits, pigs
- cattle, sheep, goats
- horses

CNS Toxicities

COMPOUND 1080

Mechanism of Action: (classical theory)

Kreb's
Cycle
(TCA)



CNS Excitation Toxicities

COMPOUND 1080

Toxic effects are variable:

- Primates and herbivores
 - Primarily a Cardiac dysfunction
- Cats, sheep and pigs
 - Cardiac and nervous effects
- Carnivores (e.g. dogs)
 - Primarily nervous signs/effects

CNS Excitation Toxicities

COMPOUND 1080

Clinical Signs/effects in the dog:

- Vocalisation, Running
- Tetanic-like seizures
- Frequent defaecation, urination
- Metabolic Acidosis
- Hyperthermia
- ↑ Blood glucose, ↓ Calcium (ionised)

CNS Excitation Toxicities

COMPOUND 1080

Clinical Signs/effects in herbivores:

- Stagger, tremble
- Signs of gastrointestinal upset
- May resemble hypocalcaemia in dairy cattle
- Cardiac arrhythmias
- Stress or exercise precipitates death
- Terminal convulsions

CNS Excitation Toxicities

1080

Clinical Pathology:

- Hyperglycaemia (2 fold or greater)
- Hypocalcaemia (ionised calcium)
- Increased serum citrate
- Metabolic acidosis

CNS Excitation Toxicities

1080 TREATMENT:

- Decontaminate if no clinical signs
- Anticonvulsants (diazepam or barbiturates)
- Metabolic Acidosis
 - Sodium Bicarbonate (fluids)
- Acetamide (fluids)
- Supportive Care

CNS Excitation Toxicities

1080 Post mortem & Diagnosis:

- Non-specific changes
- Agonal heart changes
- Rapid onset of rigor mortis
- Analysis of stomach contents **
- History of exposure

CNS Excitation Toxicities

1080 Summary:

- Clinical signs for dogs - excitation
- Effects on herbivores - cardiac
- Metabolic acidosis - Sodium Bicarb
- Rapid onset of rigor mortis
- Clin Path changes (glucose, Calcium)
- Symptomatic care & acetamide

CNS Excitation Toxicities

Metaldehyde

Sources of Metaldehyde:

- ∞ Slug or snail bait
- ∞ Pelleted mixture
 - ∞ dyed blue-green or
 - ∞ non-dyed pellets



CNS Excitation Toxicities

Metaldehyde

Toxicity of Metaldehyde:

- ∞ Dog: 200 mg/kg (but variable)
- ∞ Cattle, sheep: 200-300 mg/kg
- ∞ Bittering agent added to deter ingestion
 - ∞ But it is not 100% effective in stopping ingestion (eg dogs)

CNS Excitation Toxicities

Metaldehyde

Mechanism of Action:

- ∞ Unknown - only partly understood
- ∞ Affects CNS neurotransmitters
- ∞ Onset can be minutes after ingestion,
but may be after 1-2 hours

CNS Excitation Toxicities

Metaldehyde

Clinical signs - dogs, cats:

- Anxiety, grimacing, restlessness
- Depression
- Vomiting and diarrhoea
- Salivation
- Muscle tremors “shake and bake”
- Incoordination

CNS Excitation Toxicities

Metaldehyde

Clinical signs - dogs, cats:

- Blindness
- Metabolic Acidosis
- Excitation to narcosis
- Tachycardia, Tachypnoea
- Cats-nystagmus, convulsions stimulated
- Surviving animals may develop liver/renal disease

CNS Excitation Toxicities

Metaldehyde

Clinical signs - Herbivores:

- Ataxia, tremors
- Colic, diarrhoea
- Blindness
- sweating
- hyperthermia
- Tachycardia, Tachypnoea
- Salivation

CNS Excitation Toxicities

METALDEHYDE

Clinical Pathology

Metabolic Acidosis - check acid/base

In cases of moderate to severe toxicity:

Liver enzymes may increase

Renal tests (urea nitrogen, creatinine) increase

Diagnosis:

Submit frozen stomach contents (or vomit)

CNS Excitation Toxicities

METALDEHYDE

TREATMENT

- Metabolic Acidosis
 - (corrects itself when tremors are controlled)
- Symptomatic and Supportive Care
- Anticonvulsants (as needed)
 - Diazepam
 - Methocarbamol (Robaxin)**
 - Barbiturates

CNS Excitation Toxicities

CHOCOLATE

- methylxanthine
 - theobromine
- chronotropic and inotropic cardiac effects
- causes diuresis (like coffee)
- dark chocolate more toxic than milk chocolate



CNS Excitation Toxicities

CHOCOLATE

- Hyperactive, restless, vomiting
- Hyperthermia
- Urinary incontinence
- Hyperreflexive
- Cardiac arrhythmias
- Ataxia, seizures and coma



CNS Excitation Toxicities

CHOCOLATE TREATMENT

- Anticonvulsants
- Symptomatic and supportive care
- Premature Ventricular Contractions - lignocaine
- Tachycardia - beta blockers if persist

CNS Excitation Toxicities

RYEGRASS STAGGERS

SOURCE

- ∞ Mycotoxin - Lolitrem B
(*Neotyphodium lolii*)
- ∞ Ryegrass pastures
(*Lolium perenne*)



CNS Excitation Toxicities

RYEGRASS STAGGERS

Clinical Signs

- ∞ Trembling, twitching of muscles
- ∞ Head nodding, jerky movements
- ∞ Incoordination, ataxia
- ∞ Severe - opisthotonus

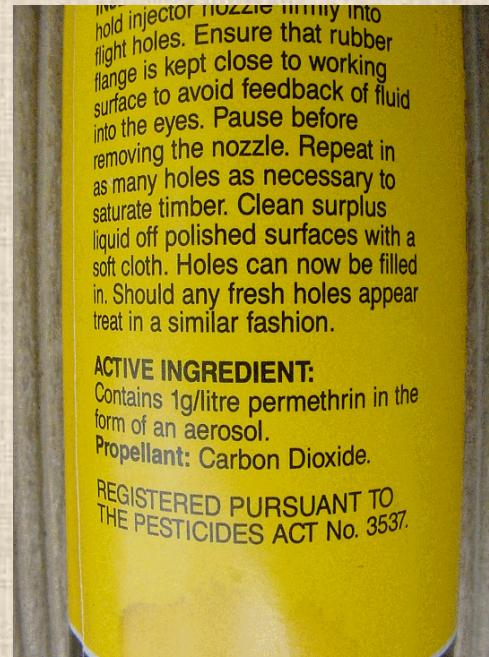
CNS - MIXED EFFECTS

PYRETHRINS OR PYRETHROIDS



CNS - MIXED EFFECTS PYRETHRINS OR PYRETHROIDS

- Numerous sources
'safe' insecticides
- popular



CNS - MIXED EFFECTS

PYRETHRINS OR PYRETHROIDS

Clinical Signs:

- Cats - very sensitive to permethrin
- Ear twitching
- Muscle tremors
- Dyspnoea
- Hyperthermia (muscle activity)

CNS - MIXED EFFECTS

PYRETHRINS OR PYRETHROIDS

Mechanism of Action:

- Act on sodium channels (Na in/ K out)
 - "open channel blockers"
- Results in repetitive nerve impulses
- Type II - GABA, glutamic acid receptors
 - leads to hyperexcitability of nervous tissue

CNS - MIXED EFFECTS

PYRETHRINS OR PYRETHROIDS

Treatment:

- Decontaminate
 - Dermal - thoroughly wash animal
 - Oral - activated charcoal & laxative
- Symptomatic & Supportive therapy
 - watch body temperature
- Anticonvulsants - prefer methocarbamol (Robaxin®) 55-220mg/kg to effect

CNS - MIXED EFFECTS PYRETHRINS

SUMMARY:

- Common and 'safe' insecticides
- Reversible effect on sodium ion channels
- Thoroughly decontaminate!
- Symptomatic care - anticonvulsants
- DO NOT use dog products on CATS

CNS - MIXED EFFECTS LEAD

Sources:

- Paint
- Leaded gasoline
- Lead shot
- Roofing nails etc
- Batteries



LEAD POISONING

Toxicity:

- Variable as lead is poorly absorbed
- Toxicity increased in young animals
- Most species - esp dogs and calves
- All species are susceptible
- Acute oral dose from 50-900mg/kg

CNS - MIXED EFFECTS LEAD

Mechanism of Action:

- Exact mechanism not known
- Toxic to enzymes, tissues, organs
 - Inhibits delta-amino levulinic acid dehydrase
- Nervous, gastrointestinal and haematopoietic tissues affected

CNS - MIXED EFFECTS

LEAD - Dog

Clinical Signs:

- GI signs: vomiting, anorexia, colic
- Lethargy
- Seizures (& chomping fits)
- Hysterical barking, hyperexcitable
- Paraplegia, loss of coordination
- Blindness
- Megaesophagus

CNS - MIXED EFFECTS

LEAD - Cat

Clinical Signs:

- GI signs: vomiting and anorexia
- Lethargy
- Depression

CNS - MIXED EFFECTS

LEAD - Cattle

Clinical Signs:

- Acute poisoning (calves):
 - Sudden death or stagger, vocalise, chomping, eye rolling, frothing
- Subacute (usually adult):
 - anorexia, ataxia, blindness, salivation, muscle tremors and hyperaesthesia
 - abdominal pain, rumen atony, constipation

CNS - MIXED EFFECTS LEAD

Clinical Pathology:

- Basophilic stippling of RBCs
- Blood lead levels
- Urinary lead
- Delta-aminolevulinic acid (urine)
- Radiographic evidence of lead

CNS - MIXED EFFECTS LEAD

TREATMENT:

- Decontamination (magnesium sulphate)
- Chelation therapy
 - Calcium EDTA - parenteral
 - D-Penicillamine - oral
- Anticonvulsants
- Supportive therapy
- Thiamine in cattle

CNS - MIXED EFFECTS LEAD

SUMMARY:

- Numerous environmental sources
- Decontamination MUST remove lead
- Gastrointestinal and neurological signs
- Chelation therapy
- Anticonvulsants
- Supportive therapy

CNS Toxicities

SUMMARY

- Decontamination & Elimination
- “Treat the patient not the poison”
- Good nursing care is IMPORTANT!

OTHER LESS FREQUENTLY SEEN TOXICITIES

STRYCHNINE no longer sold in NZ

ORGANOCHLORINE PESTICIDES

ILLEGAL DRUGS

Amphetamines and Cocaine

CNS Excitation Toxicities

STRYCHNINE

(aka nux vomica)

Infrequent poisonings as no longer sold in NZ as
a rodenticide

Nux vomica is used as a stimulant in Ketovet®

- Muscle rigidity
- Sawhorse stance
- Opisthotonus
- Violent seizures (stimulated)

CNS Excitation Toxicities

STRYCHNINE TREATMENT

- Anticonvulsants
- Symptomatic and supportive care
- Dark, quiet environment

CNS Excitation Toxicities

ORGANOCHLORINE PESTICIDES

Limited availability in NZ

- Behaviour: agitated and aggressive
- Spastic gait
- Blepharospasms
- Muscle fasciculations (head first)
- Continuous chewing
- Tonic-Clonic convulsions
- Other signs: weakness, paraesthesia

CNS Excitation Toxicities

ORGANOCHLORINE TREATMENT

- Light sedation with anaesthetics
- Symptomatic and supportive care
- Oxygen