

Veterinary and Clinical Treatment of Vertebrate Pesticide Poisoning – a Technical Review

Alan Shlosberg¹ and Lynn Booth²

¹ Kimron Veterinary Institute
PO Box 12, 50250 Bet Dagan
Israel

² Landcare Research
PO Box 69, Lincoln 8152
New Zealand

A review of treatments for toxicoses in pets caused by vertebrate pesticides (1080, cyanide, anticoagulant rodenticides, cholecalciferol, phosphorus, zinc phosphide) in New Zealand, including an updated technical overview of treatment protocols and first aid for use by veterinarians, pet-owners, and pest control operators in cases of accidental poisoning. First aid protocols for human toxicoses are also detailed.

CONTENTS

Foreword	7
Section 1: Introduction	8
Non-target poisoning	8
Primary non target poisoning	8
Secondary non-target toxicoses	9
Diagnosis of toxicoses	9
General approach to treatment of poisoning in animals	10
First responder in VP toxicoses	11
Eye and skin exposure	11
Oral exposure.....	11
General support	12
Decontamination in VP toxicoses	12
Emesis.....	13
Gastric lavage (stomach washing).....	13
Activated charcoal	14
Cathartics	14
Specific treatment of VP toxicoses.....	14
Supportive care for VP toxicoses	15
Respiratory system	15
Cardiovascular system.....	16
Blood examinations	17
Core body temperature	18
Seizures.....	19
Consciousness.....	19
Pain and comfort.....	19
References	20
Section 2: Specific toxicants and treatment regimes	22
Sodium monofluoroacetate (1080)	22
Key points.....	22
Sources of poisoning	23
Bait	23
Secondary poisoning	24
Toxicology and pathology	24
Toxicity.....	24
Absorption, metabolism and excretion.....	24
Mode of action.....	25
Non-target effects	25
Diagnosis of 1080 poisoning	25
Onset of clinical signs	25
Clinical signs	25
Laboratory diagnosis	26
Treatment of 1080 poisoning in animals	26
References	28
Cyanide	29
Key points.....	29
Sources of poisoning	29

Bait	29
Secondary poisoning	30
Toxicology and pathology	30
Toxicity.....	30
Absorption, metabolism and excretion.....	30
Mode of action.....	31
Non-target effects	31
Diagnosis of cyanide poisoning.....	31
Onset of clinical signs	31
Clinical signs	31
Laboratory diagnosis	32
Treatment of cyanide poisoning in animals.....	33
References	34
Brodifacoum.....	35
Key points.....	35
Sources of poisoning	36
Bait	36
Secondary poisoning	37
Toxicology and pathology	37
Toxicity.....	37
Absorption, metabolism and excretion.....	38
Mode of action.....	38
Non-target effects	38
Diagnosis of brodifacoum poisoning.....	39
Onset of clinical signs	39
Clinical signs	39
Laboratory diagnosis	40
Treatment of brodifacoum poisoning in animals.....	41
References	43
Other second-generation anticoagulant rodenticides.....	45
Flocoumafen.....	45
Key points.....	45
Bromadiolone.....	46
Key points.....	46
Difethalione	47
Key points.....	47
Pindone	48
Key points.....	48
Sources of poisoning	49
Bait	49
Secondary poisoning	49
Toxicology and pathology	49
Toxicity.....	49
Absorption, metabolism, and excretion.....	50
Mode of action.....	50
Non-target effects	50
Diagnosis of pindone poisoning	50
Onset of clinical signs	50

Clinical signs	50
Laboratory diagnosis	51
Treatment of pindone poisoning in animals	51
References	51
Other first-generation anticoagulant rodenticides	52
Coumatetralyl	52
Key points.....	52
Sources of poisoning	53
Bait	53
Secondary poisoning	53
Toxicology and pathology	53
Toxicity.....	53
Absorption, metabolism, and excretion.....	53
Mode of action.....	53
Non-target effects	53
Diagnosis of coumatetralyl poisoning	54
Onset of clinical signs	54
Clinical signs	54
Laboratory diagnosis	54
Treatment of coumatetralyl poisoning in animals	54
References	54
Diphacinone.....	55
Key points.....	55
Sources of poisoning	56
Bait	56
Secondary poisoning	56
Toxicology and pathology	56
Toxicity.....	56
Absorption, metabolism, and excretion.....	56
Mode of action.....	56
Non-target effects	57
Diagnosis of diphacinone poisoning	57
Onset of clinical signs	57
Clinical signs	57
Laboratory diagnosis	57
Treatment of diphacinone poisoning in animals	57
References	57
Cholecalciferol	58
Key points.....	58
Sources of poisoning	59
Bait	59
Secondary poisoning	59
Toxicology and pathology	59
Toxicity.....	59
Absorption, metabolism, and excretion.....	60
Mode of action.....	60
Non-target effects	60
Diagnosis of cholecalciferol poisoning	61

Onset of clinical signs	61
Clinical signs	61
Laboratory diagnosis	61
Treatment of cholecalciferol poisoning in animals	62
References	64
Phosphorus.....	66
Key points.....	66
Sources of poisoning	67
Bait	67
Secondary poisoning	67
Toxicology and pathology	67
Toxicity.....	67
Absorption, metabolism, and excretion.....	67
Mode of action.....	67
Non-target effects	68
Diagnosis of phosphorus poisoning.....	68
Onset of clinical signs	68
Clinical signs	68
Laboratory diagnosis	68
Treatment of phosphorus poisoning	69
References	70
Zinc phosphide.....	71
Key points.....	71
Sources of poisoning	71
Bait	72
Secondary poisoning	72
Toxicology.....	72
Toxicity.....	72
Absorption, metabolism, and excretion.....	72
Mode of action.....	72
Non-target effects	73
Diagnosis of zinc phosphide poisoning.....	73
Onset of clinical signs	73
Clinical signs	73
Laboratory diagnosis	73
Treatment of zinc phosphide poisoning in animals.....	74
References	75
Section 3: First aid in human intoxications.....	76
General first-aid notes	76
Recognising pesticide poisoning	76
General principles for treating acute pesticide poisonings.....	77
Induction of vomiting as a first-aid measure.....	77
References	79
Section 4: Signs and symptoms of poisoning and first aid for specific vertebrate pesticides.....	80
1080.....	80
Signs and symptoms	80
Toxicity to humans	80

First-aid treatment for 1080 poisoning	81
References	81
Cyanide	83
Signs and symptoms	83
Severity of poisoning (Meredith et al. 1993).....	83
Acute effects (route of exposure)	83
Inhalation.....	83
Ingestion	84
Skin.....	84
Eye.....	84
Injection.....	84
First-aid treatment for cyanide poisoning.....	84
Poisoning management discussion	85
References	86
Anticoagulant rodenticides	87
Signs and symptoms	87
Acute effects (route of exposure)	87
Inhalation.....	87
Skin.....	87
Toxicity.....	87
First-aid treatment for anticoagulant poisoning	88
References	88
Cholecalciferol	90
Signs and symptoms	90
Toxicity.....	90
First aid treatment for cholecalciferol poisoning.....	90
References	91
Phosphorus	92
Signs and symptoms	92
Acute effects (route of exposure)	92
Ingestion	92
Skin.....	92
Chronic effects.....	93
Inhalation.....	93
Toxicity.....	93
First-aid treatment for phosphorus poisoning.....	93
References	94
Zinc phosphide.....	95
Signs and symptoms (acute).....	95
Toxicity.....	95
First-aid treatment for zinc phosphide poisoning.....	95
References	96
Section 5: Pictures of baits.....	97
Section 6: Recommended basic kit for veterinarians	101

Foreword

New Zealand's mammalian pest problems are unique in the world. The application of toxic baits is one effective means of controlling these pest populations. Continued use of these toxicants in the short-term at least, is essential in order to maintain our economic health, meet our international obligations for biodiversity protection, and maintain the natural heritage of our forest landscapes. The active ingredients of these baits, sodium monofluoroacetate (1080), cyanide, cholecalciferol, anticoagulants, phosphorus, and zinc phosphide, will be referred to as vertebrate pesticides (VP) in this manual.

No toxicant is absolutely safe to non-target animals, and incorrect or imprudent use of VP exacerbates risk of unintentional exposure. It is the aim of this technical manual to help veterinarians more effectively treat animals unintentionally poisoned (through primary or secondary exposure) following application of VP for pest animal control. The information in this work has been gleaned from a number of experimental and field sources, as well as from experience gathered from clinicians worldwide.

Although this manual puts emphasis on the veterinary treatment of poisoned animals, an updated account of first aid treatment of poisoning in humans is included (Sections 3 and 4).

This review does not detail treatment for all the pesticides that can poison non-target animals, and the diagnosis and treatment of toxicoses from other pesticides (including insecticides, herbicides and fungicides) are detailed elsewhere. This work deals with domestic non-target species that can be effectively treated, that is, pet dogs and cats, and first aid in humans. Diagnosis and treatment in other domestic or wildlife non-target animals, especially birds, is more difficult. It should also be realised that animals may occasionally be exposed to VP formulations no longer in use, which may confound diagnosis.

Section 1: Introduction

The focus of this review is on the treatment of toxicoses caused by poisons used for the control of introduced mammals that are considered pests in New Zealand (NZ). Intensive measures have been devised, and implemented widely in NZ, to control a variety of introduced mammalian pests. These include, for example, aerial application of 1080 bait for possum control on mainland NZ, and also of baits containing brodifacoum for rodent eradication on offshore islands. Such necessary measures are amongst the most comprehensive and aggressive taken worldwide to control introduced mammals, and the subsequent results have proved their worth. The risk to non-target species will be determined by the intrinsic susceptibility of the various species, the properties of the toxicants used (such as their toxicokinetics), the bait formulation, and the way in which toxic baits are used in the field, which may preclude, limit or increase the exposure of non-target species. This technical manual documents in detail the properties of the various poisons relevant to risk of accidental poisoning. All toxicants have advantages and disadvantages, which make them more or less effective or appropriate for different use patterns. A large database of global literature has been compiled on these compounds, which has been complemented by NZ-based research. Much of the information (and the basis of this work) was detailed (with full references) in the Department of Conservation Technical Series guide “*Vertebrate Pesticide Toxicology Manual (Poisons)*” (2001).

Non-target poisoning

Primary non target poisoning

The various toxic preparations intended as VP have been specifically formulated to target certain pest species. Clear label instructions for use aim to cause maximum mortality to target species yet pose a minimal hazard to non-target animals (NTAs). However, biology is very variable, and although trials may indicate that some baits are unattractive to NTA, in the field there will always be individuals that differ, and these may even influence the feeding behaviour of cohorts of the same or different species. Bait formulations can also be misused, either unintentionally or intentionally and not according to label instructions, e.g. higher delivery density, incorrect habitat baited, or maliciously), so increasing the risk to NTA. Once the NTA has an opportunity to eat the

bait, the attractiveness of that bait will largely determine the risk of a definite exposure to the toxicant. Most VP baits in NZ are for herbivore and omnivore control (although cats, ferrets and stoats are target species of some baiting operations). Dogs may occasionally take baits laid for herbivorous pests.

Secondary non-target toxicoses

Secondary poisoning can occur when a "targeted" animal is consumed by a NTA and thereby is exposed to toxic residues in the animal. This may be from remnants of the toxicant in the gastrointestinal tract of the pest (e.g. zinc phosphide in the stomach), or residues in organs (e.g. brodifacoum in the liver or fluoroacetate from 1080 in the muscles). Target animals in the latter stages of poisoning are likely to be debilitated and easier for predators to catch. The likelihood of the NTA eating poisoned (dead or dying) target species will largely determine the risk of secondary poisoning. This is partially determined by the innate behaviour of the NTA, and also sensitivity to the toxicant (as indicated by the oral LD₅₀). Dogs are likely to be less selective than cats. Such secondary toxicoses are a significant threat to predators, including birds of prey and carrion-eaters. This manual gauges the likelihood of each toxicant to cause secondary poisoning.

Diagnosis of toxicoses

Making a correct diagnosis is essential before starting specific treatment for poisoning, where treatments may require injection of substances that are themselves potentially toxic. If the initial diagnosis is wrong, the corresponding treatment may prove to be harmful or even fatal (e.g. dicobalt edetate or nitrite for cyanide poisoning). Correct diagnosis is not easy for all toxicoses. Often the differential diagnosis is arrived at by a process of due diligence and elimination whereby the vet rules out infection/metabolic/inflammatory causes etc, and after inquiry identifies possible VP exposure. Information on vertebrates poisoning pesticide operations should be available from local regional councils or Department of Conservation offices.

A diagnosis is best made on the history of the suspect poisoning incident, the occurrence of clinical signs from a thorough clinical examination, and the results of laboratory examinations. A history of the incident may uncover knowledge of a recent

baiting campaign, or a pattern of similar cases where dead or dying animals have been found. Few toxicoses have signs that are characteristic of a disease, but some toxicants do have discriminative clinical signs, (e.g. 1080 in dogs), and these may vary between species. Anticoagulant pesticides (e.g. brodifacoum, pindone) are unique in that the location and extent of the haemorrhage largely determines clinical signs (and prognosis) and so such toxicoses are difficult to diagnose. Many toxicoses show signs in the gastrointestinal and nervous systems, with vomiting, diarrhoea, depression and seizures being particularly common. These signs are also readily recognisable to non-veterinarians.

However, the urgent necessity of treatment in near-moribund animals may preclude the last two important stages (comprehensive clinical and laboratory examinations) in any diagnostic protocol. Examination of the various body systems will invariably add to the clinical database and so aid diagnosis. Laboratory testing is essential in providing strong evidence or proof of poisoning. This usually comprises testing both the suspect bait and some part of the animal (vomit, stomach-washings, blood, faeces, or urine in live animals, and stomach contents or liver most often in dead animals) to confirm exposure. However, a positive result indicates exposure but not necessarily a lethal toxicosis (e.g. brodifacoum liver residues), and the absence of detectable residues does not necessarily confirm that no exposure occurred (e.g. cyanide). Chemical analyses are usually complex, time consuming, expensive, and conducted only by specialist laboratories. A post-mortem examination can aid diagnosis by finding evidence of bait in the stomach, or characteristic pathological lesions, particularly if these are observed in several animals. Histopathology may be performed on fresh tissues, but as this takes at least several days, it will not add to the efficacy of treatment of sick animals. The costs of comprehensive diagnostic testing may often be sufficient to deter the animals' owners from pursuing a diagnosis. This is particularly so for persons submitting wild animals.

General approach to treatment of poisoning in animals

The overall treatment needs to be based on counteracting the specific effect(s) of the toxicants, and supporting the body systems to maintain vital functions. Often supportive treatments alone will succeed. Specific (antidotal) treatments do exist in veterinary

toxicology for some VPs, but for antidotes to be effective, quick diagnosis and treatment are essential, as animals may die very rapidly. This technical manual details the best ways for treating toxicoses caused by the VP toxicants 1080, cyanide, anticoagulant rodenticides, cholecalciferol, zinc phosphide, and phosphorus, allowing the reader to find the balance between optimal and practical solutions.

First responder in VP toxicoses

Treatment (first aid) should be given only by a person knowledgeable and responsible enough to take action that may save the life of the animal prior to it being brought to specialist help. This usually comprises procedures used to stop or reduce absorption and also perhaps augment elimination.

Eye and skin exposure

With some pesticides, absorption through the ocular mucous membrane or through the skin may be important, but of the toxicants in this review, only cyanide has this possibility, and even that is considered unlikely in the context of cyanide bait application for pest animal control. In such a case, if bait is seen in the eye or on the skin, it should be removed with gloved hands, put into a sealable plastic container, and disposed of appropriately. The area of contact with the bait should be washed with water, optimally for 15 minutes for the eye. After cutting off contaminated hair, skin should be washed for 5 minutes, with a small quantity of hair shampoo added. The patient may have to be mildly sedated to allow this to be properly performed without causing discomfort.

Oral exposure

Where the animal has ingested a suspected toxicant (e.g. bait or the carcass of a poisoned animal) evacuation of stomach contents is a logical first step. However, inducing vomiting is now regarded as less effective in toxicant removal than previously thought, and the process itself can be a health risk. Typically, vomiting should not be induced if more than 1 hour has elapsed since ingestion, if there has already been vomiting, or if the animal shows marked clinical signs, seizures or any loss of full consciousness. However, anecdotal evidence suggests that making the animal vomit at later stages can still sometimes be beneficial. Emetics found in the home environment

are far from reliable, but syrup of ipecac (7%) is regarded as the best, at a dosage of 1–2 ml/kg body weight (BW) for dogs and 3 ml/kg BW for cats. However, the liquid is bitter and unpleasant for the animal. Vomiting should occur in 30 minutes, but if unsuccessful, one repeat dose may be given. Ipecac may cause cardiac arrhythmia if allowed to remain in the stomach. A knob of washing soda (sodium carbonate) about 1cm in diameter is a suitable emetic. Further doses may be given safely if the first dose is not effective. Hydrogen peroxide solution (medicinal, 3%) may be more practical and safer. It should be used at a dosage of 1–3 ml/kg BW; and vomiting should occur within 15 minutes, but if unsuccessful, one repeat dose may be given. Other potential emetic agents found in the home are less reliable or may be even dangerous, and cannot be recommended; but if there is no alternative, powdered mustard in water can be tried. If activated charcoal is available, this could be carefully administered orally, and should reduce adsorption of all the VP except cyanide and perhaps zinc phosphide. The dosage given, as a suspension in water, will vary with the particular preparation used, and is detailed in the instructions given on the label.

General support

If the animal shows considerable difficulty in breathing, the mouth can be opened with gloved hands to see whether the airway might be blocked by vomit or a flaccid tongue. If any obstruction is seen, it should be carefully moved with a gloved finger or forceps. However, beware of biting that is common in hyper-excited dogs and cats. Convulsing animals should be protected from physical damage. Restrain animal properly so that transport is safe for unconscious animals.

Decontamination in VP toxicoses

Once the animal is brought to a clinic, specialist treatment can begin to reduce exposure and increase elimination of the toxicant. It is most helpful for the veterinarian to know what the poison might be (presence of label, or bait), when it might have been ingested, and which first-aid procedures, if any, were previously attempted. All baits or suspicious materials should be put into sealed, labeled containers and should not be handled with bare hands.

Emesis

If emesis is deemed worthwhile, specific emetics are more effective and have fewer side effects. For dogs, an apomorphine tablet (6.25 mg) may be placed under the lower eyelid. Emesis occurs in about 5 minutes, and the dog should be allowed to vomit for as long as necessary. The tablet is removed and the subconjunctival sac is washed with saline for 2–3 minutes (it is irritant to conjunctiva). An injectable apomorphine preparation can be given at a dosage of 0.04–0.08 mg/kg intramuscularly (IM) or 0.02–0.04 mg/kg intravenously (IV). For cats, xylazine is preferred, at a dosage of 0.5–1 mg/kg given IM. Vomiting usually commences within 10–15 minutes. In some cats xylazine may cause respiratory depression and bradycardia, but this can be successfully treated with its antagonist, yohimbine, administered at 0.1 mg/kg IV.

Gastric lavage (stomach washing)

This relatively complex procedure is often the first choice of a well-organised practice, allowing in addition to poison removal, the administration of activated charcoal and a cathartic (see below). It is highly preferable to induction of vomiting, but may also be used shortly after unsuccessful attempts at vomiting or where vomiting is contraindicated. There is little benefit to be gained by administering lavage more than 3–4 hours after ingestion. To administer, the patient is lightly anaesthetised and a cuffed endotracheal tube is inserted to avoid aspiration from the stomach. Measurement must be made of the distance from the tip of the nose to the xiphoid cartilage and the stomach tube marked accordingly. The end of the tube should project at least 5 cm beyond the animal's nose to avoid reingestion and contact with oral mucosa. One, but preferably two, stomach tubes are inserted; a small bore tube through which to insert the lavage fluid, and a large bore tube (approximately the same size as the endotracheal tube) to allow easy flow from the stomach. Before lavage, it must be checked that the tube is in the stomach. The animal is positioned in right-side recumbency with the head position lowered (by tilting the table no more than about 20 degrees). Warm (37°C) water is passively infused through the small tube at a dosage of 5–10 ml/kg BW and allowed to flow out of the larger bore tube, after massage of the stomach area. The first wash should be kept for possible toxicological analysis. This washing should be repeated until the fluid obtained is clear (usually at least 10 cycles).

Activated charcoal

Orally administered activated charcoal (AC) can adsorb many toxicants in the gastrointestinal tract, particularly large non-polar compounds, and would logically be an effective treatment for VP poisoning except for cyanide and zinc phosphide. It is best given after emesis or gastric lavage, but many specialists recommend AC alone in place of those potentially dangerous procedures. Once again, the sooner after ingestion it is given, the more toxicant will be bound and effectively neutralised. Specific commercial preparations of powdered activated charcoal are given as a 20% suspension in tap water at a dosage of 5 g of the slurry/kg BW, by gavage or stomach tube. Repeat doses can be given every 4-6 hours. Sedation and the use of a cuffed endotracheal tube are needed to avoid aspiration.

Cathartics

Substances that stimulate rapid elimination of intestinal contents remove free toxicant and also any toxicant bound to charcoal (which might partially desorb in the intestines). Of the available cathartics, sorbitol is preferable, being without side effects and also having a readily acceptable taste. It is given at a dosage of 3 mg/kg BW, and is best mixed with the activated charcoal. Ready-to-use charcoal + sorbitol combinations are available commercially. Sodium sulphate is an acceptable alternative, preferably given about 1 hour after the charcoal, at a dosage of 0.25 g/kg in 5–10 times as much water. Care must be taken to avoid consequent dehydration.

Specific treatment of VP toxicoses

In asymptomatic patients suspected of ingesting toxicants, a comprehensive history and physical examination will aid in assessing whether there has been an exposure. Initial procedures that may later facilitate diagnosis and treatment comprise taking blood samples (serum, plasma), establishing access to a vein, and inserting a urinary canula. Intensive monitoring of vital systems should be performed initially, with routine blood and urine testing. If the suspect VP has been identified, monitoring should concentrate on the organ systems characteristically affected and the typical clinical manifestations shown, in order to gauge when to start more aggressive treatment in addition to general supportive measures.

This manual provides a protocol comprising various combinations of general treatment, specific (antidotal), and supportive measures will be detailed for each particular VP. Specific antidotal treatment is limited to the anticoagulants (e.g. brodifacoum) and cyanide.

Supportive care for VP toxicoses

The availability of antidotal treatment is usually an uncommon bonus when dealing with NTA poisoning cases. Accordingly, procedures and protocols to aid patients to overcome primary and secondary biochemical, physiological and pathological changes affecting homeostasis of the body systems are well developed and should be fully utilised, even together with antidotal treatment. Very often, symptomatic and supportive treatments are the only measures taken when diagnosis is uncertain. The level, intensity and duration of supportive care depend largely on the resources and effort that can be expended. This manual will detail the most practical of the possible procedures for VP.

Respiratory system

Respiratory failure is probably the most important single cause of death in poisoning, but can often be prevented. Primary compromise to respiratory function can be caused by physical obstruction of ventilation, reduced breathing efficacy (ventilatory failure, hypoxia, bronchospasm), a central depression, or harmful effects secondary to primary changes in the cardiovascular system. Maintenance of a patent airway, adequate ventilation and prevention of aspiration of vomit are crucial steps. If the animal is unconscious or anaesthetised, a cuffed, inflated, endotracheal tube may be inserted. If necessary, assisted ventilation can then be given.

Physical obstruction of airway can be a consequence of exaggerated tongue flaccidity, excessive fluid production or the presence of vomit. These abnormalities would cause great difficulty in breathing, usually manifested by abnormal sounds of respiratory distress and stridor and visibly hypoxaemic mucous membranes.

Ventilatory depression or failure is caused by insufficient respiratory muscular activity, or central nervous system (CNS) depression of respiration. Monitoring is done by observing respiratory activity and by measuring the arterial blood gas pressure (PaCO₂, PaO₂) and/or the oxygen saturation of haemoglobin in arterial blood (SpO₂). The SpO₂ is most easily determined by using pulse oximeters. Oxygen administration is essential

in most cases of acute poisoning particularly when no means of monitoring arterial blood gas pressure or pulse oximetry is available – oxygen has beneficial effects on heart and lung tissues and helps in alleviating metabolic acidosis. Oxygen supplementation is nearly always of great help and should be routinely used. Low blood oxygen can also be a result of acute poisoning, due to pulmonary oedema (e.g. due to phosphine from zinc phosphide) or chronic poisoning, due to aspiration pneumonia after vomiting, secondary to blood loss (e.g. anticoagulants), or by cellular hypoxia (cyanide). Rapid and thorough oxygen administration is essential in such cases.

Changes in the acid-base balance are frequent in toxicoses, and can have serious repercussions if not rapidly corrected, and so should be well monitored. This may not be possible in an average veterinary practice. Respiratory acidosis is most often seen and can be corrected with infusion of bicarbonate.

Cardiovascular system

Primary or secondary damage to the function or integrity of the heart and blood vessels commonly occurs in many toxicoses, including those dealt with here. Monitoring and assessment of system function, involving tissue perfusion, can be done by several methods.

Mucous membrane colour deviations from pink are easily seen. A bright red colour may be seen with cyanide poisoning and a marked pallor with anticoagulants.

Pulse rate, rhythm and quality may be abnormal; if normal these parameters can be crude monitors of cardiovascular system function.

Capillary refill time, measured on gingival mucosa, is normally 1–2 seconds, but may be longer in cases with marked dehydration and poor circulation (shock).

Lactate concentrations in serum may be useful as an aid to assess tissue perfusion. Increased values (normal < 1-2 mmol/litre) may indicate poor tissue oxygenation.

Heart examinations can pinpoint abnormalities of cardiac function that may have led to the reduced perfusion. Electrocardiography may add specific details of cardiac malfunction, particularly arrhythmias, and should be used when monitoring anaesthetised animals. Arrhythmias signify in many cases that the myocardium is

compromised and in most cases of poisoning they are secondary to hypoxia. Echocardiography can assess inotropic status that may affect heart output.

Blood pressure Doppler-based blood pressure measurement is fairly easy to do. The “Memoprint” is a machine that does all measurements of blood pressure automatically. Clinically, a comparison is made of the pulse in the plantar, dorso-metatarsal and femoral arteries; the more distal the measurement, the lower the pulse. Differences disappear from distal to proximal when hypotension develops. Hypotension, manifested as shock and circulatory collapse, is the major problem, mainly due to hypovolaemia from fluid losses (emesis, diarrhoea, polyuria). Tachycardia is often associated with hypotension. Correction of hypotension is usually carried out by administering intravenous fluids. Failure to speedily restore normal blood pressure with replacement crystalloid solutions (0.9% saline, Ringer’s solution or lactated Ringer’s solution) necessitates a rapid bolus infusion of a small dosage of isotonic crystalloids (for dogs in shock 60–90 ml/kg/hour and for cats 40–60 ml/kg/hour), followed by observation of effect and consequent administration of additional doses if required. Colloids may also be used, usually given after seeing a less than optimal therapy with previous crystalloid administration. These include Hetastarch at 10ml/kg IV given over 1–6 hours with an additional 10ml/kg given over 24 hours, or gelatin solutions (such as Hemacel) or Dextran 70 at similar dosages.

Urine output should be monitored to ensure kidney function. Urine production is normally 1–2 ml/kg BW/hour. Urine pH may be a useful guide to acid-base imbalances.

Blood examinations

If the urgency of the case permits it, blood samples should be taken as soon as the patient is admitted in order to aid in the subsequent diagnosis, treatment and prognosis. Samples for serum (electrolytes, enzymes, urea etc) are taken, with an anticoagulant, e.g. heparin, for hematology and with citrate to gauge blood-clotting abnormalities. Lactate and glucose are determined in blood taken with fluoride as an anticoagulant. Further samples may be taken during the course of the treatment to assess treatment efficacy, development of recovery and future therapy.

Hematological examinations are important to gauge homeostasis and the degree of hydration. A low haematocrit may point to internal bleeding, whereas an elevated value

may signal dehydration (total protein is a much better and more sensitive indicator of bleeding as changes in PCV tend to be compensated by splenic contraction). The most sensitive test to assess the integrity of coagulation activity after anticoagulant exposure is the prothrombin time test (PT). The PIVKA (proteins induced by vitamin K antagonists) test is also good and may in the future be the test of choice, whereas the activated partial thromboplastin time (APTT) test will detect anticoagulant poisoning in cases a little more progressed. Prolonged PT and normal APTT values are specific for this type of poisoning.

Electrolyte abnormalities in sodium, potassium and calcium serum concentrations are frequently recorded in cases of poisoning and so these ions should be monitored. Significant changes in sodium usually indicate alterations in total body water. Hypokalaemia is a common consequence of protracted vomiting, diarrhoea or polyuria. Hyperkalaemia may also be seen in poisoning after cellular damage. Changes in calcium are uncommon in most cases of poisoning, except that the rodenticide cholecalciferol causes a characteristic severe hypercalcaemia. Ionised calcium is the preferred measurement compared to total calcium.

Core body temperature

Both hyperthermia and hypothermia can be harmful but are easily monitored and corrected. Hyperthermia with VP is most likely consequent with the terminal seizures characteristic of 1080 in dogs, but is common in many toxicoses with excessive muscular activity. Correction of moderate hyperthermia (up to 40.5°C) is best done by cold-water immersion or wetting the animal with running tap water and not allowing the fur to dry. A fan can be used for cooling wet fur, and in extreme cases cooling can be expedited using 70% alcohol with a fan. Severe hyperthermia may necessitate colonic irrigation with cool water. Continuous monitoring of core temperature is done to prevent consequent hypothermia, and cooling is stopped when core temperature reaches 39.0°C. Hypothermia is not seen as a specific effect of any of the VP, but is frequently seen in cases of poisoning. Temperatures <36.5°C should be treated by vigilant and gradual re-warming with controlled temperature water-heated blankets and a warm (35–38°C) ambient temperature; e.g. using warm air blowers. Heating is stopped when core temperature reaches 38.0°C. A difference between toe-web and core temperature may indicate poor blood circulation.

Seizures

May be mild, or severe and life threatening. They may induce vomiting (with possible aspiration pneumonia), cause hyperthermia, respiratory or metabolic acidosis, hypoxaemia, hyperkalaemia, and rarely rhabdomyolysis (with possible kidney damage). With the VP, seizures seen in 1080 poisoning in dogs are the most important manifestation that leads directly to death by impairment of respiration, and their control is a prerequisite for successful treatment. Control of seizures is attempted once an open airway is ensured. Different anticonvulsants can be used with diazepam (0.25–1.00 mg/kg IV) probably being the most useful and safest in mild cases. With severe convulsions, induction of general anaesthesia is preferable, using diazepam. If response is insufficient, phenobarbital at 2–4 mg/kg IV, or pentobarbitone at 6 mg/kg IV initially and then, if necessary, to effect by drip at 60 mg + 6 mg diazepam in 100 mL lactated Ringer's solution at a slow "to effect" continuous drip can be used. Alternatives comprise the muscle relaxants methocarbamol or glycerol-guaiacolate at 40–110 mg/kg IV to effect and later by drip, or gaseous anesthesia such as isoflurane or halothane via a mask or preferably via tube.

Consciousness

Lowered levels are induced in many toxicoses by primary or secondary effects on the brain. Adequate blood oxygenation through respiratory and cardiovascular function should be evaluated. Fluids are given to maintain blood pressure and adequate hydration. Normal core temperature is ensured. Blood glucose levels can be examined to check for hypoglycaemia.

Pain and comfort

Several of the VP may induce pain or suffering that, apart from welfare considerations, may also alter behaviour of the animals (hyperactivity), which may exacerbate the poisoning. Treatment with analgesics, tranquilisers (diazepam 2.5–10.0 mg/kg to effect) or anaesthesia may help, but should only be used when assessed as not impinging on life-threatening processes. The potent synthetic opioid fentanyl is available as dermal patches for pets. Hospitalising the patient in a warm, quiet, preferably dark, comfortable environment with frequent owner visits will help to hasten recovery.

References

Campbell, A.; Chapman, M. 2000: Handbook of poisoning in dogs and cats, Blackwell, UK.

Dorman, D.C. 1995: Emergency treatment of toxicoses. *In: Kirk's current veterinary therapy*, vol. XII Small animal practice, W.B. Saunders, Philadelphia, USA. Pp. 211-217.

Drellich, S.; Aldrich, J. 2001: Initial management of the acutely poisoned patient. *In: Peterson, M.E.; Talcott, P.A. eds Small animal toxicology*. W.B. Saunders, Philadelphia, USA. Pp. 33–47.

Eason, C.T.; Wickstrom, M. 2001: Vertebrate pesticide toxicology manual (Poisons). *Department of Conservation Technical Series 23*, Department of Conservation, Wellington, NZ.

Fitzgerald, K.T. 2001: Establishing a minimum database in small animal poisonings. *In: Peterson, M.E.; Talcott, P.A. eds Small animal toxicology*. W.B. Saunders, Philadelphia, USA. Pp. 48–55.

Galey, F.D. 2001: Approach to diagnosis and initial treatment of the toxicology case, *In: Peterson, M.E.; Talcott, P.A. eds Small animal toxicology*. W.B. Saunders, Philadelphia, USA. Pp. 99–113.

Gfeller, R.W.; Messonnier, S.P. 1998: Patient evaluation and treatment of poisoning. *In: Handbook of small animal toxicology and poisonings*, 2nd edition. Mosby, St Louis, Missouri, USA. Pp. 1–64.

Mellema, M.S.; Haskins, S.C. 2001: Supportive care of the poisoned patient. *In: Peterson, M.E.; Talcott, P.A. eds Small animal toxicology*. W.B. Saunders, Philadelphia, USA. Pp. 56–84.

Osweiler, G.D. 1996: Therapy and management of toxicoses. *In: Toxicology*. Williams and Wilkins, Philadelphia, USA. Pp. 47–62.

Parton, K. 2001: The treatment of poisoning. *In: Veterinary clinical toxicology*. Massey University, NZ. Pp.12–20.

Peterson, M. 2001: Toxicologic decontamination. *In*: Peterson, M.E.; Talcott, P.A. *eds* Small animal Toxicology. W.B. Saunders, Philadelphia, USA. Pp. 85–98.

Plumlee, K. 2004: Clinical Veterinary Toxicology, Mosby, St Louis, USA.

Rosendale, M.E. 2002: Decontamination strategies. *In*: The veterinary clinics of North America: small animal practice. W.B. Saunders, Philadelphia, USA. Pp. 311–321.

Section 2: Specific toxicants and treatment regimes

Sodium monofluoroacetate (1080)

Names and structure: Sodium fluoroacetate, sodium monofluoroacetate, fluoroacetate, compound 1080 (“ten-eighty”); CH_2FCOONa .

Commercial names of bait: 1080 Pellets, 1080 Gel, 1080 Feral Cat Bait, Pestoff Professional 1080 Possum & Rabbit Paste, Pestoff Professional 1080 Possum Paste, No Possums 1080 Gel Bait.

Appearance of formulations: Cereal pellets or carrot baits, or pea-sized slugs of paste, all coloured green. See pictures in Section 5.

Key points

- In NZ, 1080 is commonly applied aerially as cereal pellets or chopped carrot baits containing or sprayed with (carrots) 0.8–0.15% 1080. The toxicant in bait may be stable in the field under cool, dry conditions for several months.
- Dogs are extremely susceptible to 1080.
- Secondary poisoning occurs in dogs and cats that eat dead or dying animals.
- Dogs exhibit distinctive signs with wild, uncontrolled running and vocalisation, followed by repetitive episodic tonic-clonic convulsions in recumbency.
- Cats show fewer characteristic signs, mainly vocalisation.
- Before signs appear, absorption may be reduced by inducing vomiting, gastric lavage, and administration of activated charcoal with a cathartic.
- Once signs are manifested, there is no point in attempting to reduce absorption.
- No practical antidotal treatment exists.

- The most important treatment is to control convulsions, thus allowing the animal to breathe and giving time for the toxicant to be excreted. Start with diazepam at 1 mg/kg with readiness to intubate. If seizures continue, pentobarbitone at 6 mg/kg IV initially and then, if necessary, by drip at 60 mg + 6 mg diazepam in 100 mL lactated Ringer's solution at a slow "to effect" continuous drip.
- Concomitant with this, intensive supportive care is given.
- Observation and treatment may have to be continued for up to 48 hours.
- There is no case evidence that single sublethal exposures to 1080 cause pathological changes in dogs or cats that endanger the health of the animal after recovery.

Sources of poisoning

Bait

Formulation and usage. 1080 is the most widely used of the VP in New Zealand when possum numbers need to be reduced rapidly over large areas. Baits (carrot, cereal, paste, and gel bait formulations) are either commercially available to licensed handlers or some types are made by licensed pest-control operators. Carrot baits for aerial distribution are chopped and screened to remove small pieces; to reduce the risk of poisoning non-target birds. Cereal pellet baits are used for both aerial and bait station control. Paste baits, and more recently gel baits, are used for ground-based follow-up maintenance control. Cinnamon is usually added to baits to mask the taste of 1080, and is thought to be a partial deterrent to birds. Green dye is also added to deter birds. Ready-to-use baits contain 0.4–2 g 1080/kg bait material, pastes 0.6–1.5 g 1080/kg, gels 1.5–100 g of 1080/kg, and liquid concentrates 200 g 1080/litre.

Availability and persistence in the environment. In comparison to cereal bait, 1080 is retained in carrot baits and will only leach slowly from carrots into the soil. Moreover, control operations are made in dry weather to prevent degradation of baits before they are accessed by target pests. Some degradation by microorganisms on the decaying baits and in the soil around baits is probable, particularly if the baits become moist. Under conditions less favourable to bait degradation, e.g. dry and/or cold, 1080 residues might persist in baits for several months. All non-target animals must be kept well away from

baits, as whole or partially degraded baits have previously caused poisoning in sheep and cattle.

Secondary poisoning

Dogs are extremely susceptible to 1080 and must be kept away from toxic baits and possum carcasses. Predators such as cats and mustelids are also susceptible to secondary poisoning. Whilst 1080 is comparatively rapidly eliminated (within days) from living animals, it can persist in carcasses for many months and may pose a risk to dogs. 1080 is taken up from baits by some terrestrial invertebrates, but persistence is short-lived and so the risk to birds or other predators is therefore confined to a short period after baiting. Large invertebrates like weta frequently eat bait and can accumulate comparatively large amounts of toxicant, and so could be a source of secondary poisoning.

Toxicology and pathology

Toxicity

While 1080 is a broad-spectrum toxin, there are some marked differences in species susceptibility. Dogs are extremely susceptible to poisoning, mammalian herbivores have intermediate sensitivity, and birds and reptiles are respectively less sensitive. The LD₅₀ (mg/kg BW) of 1080 for various species is: dog 0.07, cat 0.3, sheep 0.4, cattle 0.4, goat 0.6, horse 1, rat 1.2, possum 1.2, human 2–5, duck 9, fowl 14.

Absorption, metabolism and excretion

1080 is rapidly absorbed from the stomach and is metabolised (lethal synthesis) in cells to fluorocitrate. Peak plasma concentrations of 1080 occur approximately 0.5 hours after ingestion of sublethal 1080 doses in possums and rabbits, after 0.75 hours in goats, and 2.5 hours in sheep. This correlates with the latent period between ingestion and clinical manifestations and reflects the time taken for absorption and distribution of fluoroacetate, and the conversion of fluoroacetate to fluorocitrate. Prolonged persistence of 1080 in animals after sublethal exposure does not occur in rabbits, goats, possums, and sheep. Fluoroacetate residues are found mainly in the blood, muscle, heart and kidneys, with lower residues in the liver. Elimination is in the urine. All traces of the toxin are likely to be eliminated within 1 week following a sublethal dose.

Mode of action

The toxic metabolite fluorocitrate inhibits the tricarboxylic acid (Krebs) cycle. Toxicosis is caused by the severe inhibition of energy production, which results in either cardiac or central nervous system disorders, and secondary respiratory failure.

Non-target effects

Dogs are extremely sensitive to 1080, therefore even a taste by an inquisitive dog could be hazardous. Domestic cats are rarely poisoned by 1080 in NZ, although feral cats may be targeted by baiting operations.

Diagnosis of 1080 poisoning

Diagnosis of 1080 poisoning is based on history of exposure, clinical signs and examinations, and laboratory scrutiny and analysis (including pathology in lethal cases).

Onset of clinical signs

The latent period between the time 1080 is ingested and the appearance of clinical signs in mammals is usually 0.5–3 hours, but can be much longer. Animals receiving sublethal doses of 1080 usually show mild clinical signs of poisoning, metabolise and excrete 1080 within a few days, and show a full recovery.

Clinical signs

- Clinical signs of 1080 poisoning vary with the species affected. In general, neurotoxic signs predominate in carnivores, while herbivores show signs of cardiotoxicity. However, there are exceptions and overlapping effects in some cases.
- Poisoning in dogs is characterised by signs of anxiety followed by sudden frenzied running with wild barking, whining or howling. Affected dogs appear to be oblivious to their surroundings and owners, and may show emesis, hyperaesthesia, mydriasis and photophobia.
- The dog falls, often in a shaded place, in tonic-clonic seizures, with repeated urination and defaecation. Seizures increase in frequency and severity with time until death, apparently from respiratory failure, usually 2–12 hours after ingestion, but sometimes even up to 48 hours.

- A thorough examination of the dog does not usually add diagnostic data, as the dog presents with very typical signs. Dogs do not show the electrocardiographic changes seen in sheep that are suggestive of cardiac ischaemia. Hypotension is thought to be one of the more important predictors of mortality in 1080 intoxication.
- Clinical manifestations in cats are less severe and non-specific. Signs reported include disorientation, uncoordinated movements, excitation or severe depression, abnormal sensitivity to light and touch, vocalisation, salivation, diarrhoea; hypothermia, cardiac arrhythmia and bradycardia.

Laboratory diagnosis

- The most reliable indicators of 1080 exposure are measurement of 1080 residues in blood, skeletal or cardiac muscle tissue, stomach/rumen contents or vomit.
- Ante-mortem clinical pathology changes consistent with 1080 poisoning include increased serum citrate concentration (the most specific and reliable biomarker), hyperglycaemia, hypocalcaemia, azotaemia (increased serum urea nitrogen), and lactic acidosis (secondary to seizure activity).
- In animals that survive, clinical pathology parameters return to baseline levels by 3–4 days after exposure.
- The pathological changes observed at post-mortem appear to be largely the result of progressive hypoxaemia and cardiac failure, with venous congestion of organs, and are non-specific. The stomach, colon, and urinary bladder of dogs and cats will invariably be empty. Petechiae are often seen in the thymus and pancreas.

Treatment of 1080 poisoning in animals

1080 poisoning is an urgent medical emergency, and veterinary treatment should be initiated as soon as possible. The onset of clinical signs precludes efforts to prevent absorption. Despite many research efforts (involving acetamide, glycerol monoacetate, ethanol and acetic acid, monoacetin, and 4-methylpyrazole), no effective antidote for 1080 poisoning has been developed to practical availability. Treatment is largely symptomatic and supportive, mainly by controlling convulsive fits and allowing the toxin to be eliminated from the body. Repeated seizures may persist as long as 48 hours,

so necessitating prolonged anaesthesia. In such cases, patients should be turned over at least 4 hourly.

Therapeutic goals are (1) to decrease 1080 absorption and facilitate toxin excretion; (2) to control seizures; and (3) to support essential body functions. Recommendations for the treatment of 1080 poisoning in dogs and cats are as follows:

- When an animal is seen to eat bait or 1080-poisoned carcasses, induce vomiting of toxic material within 1 hour.
- Before the onset of any clinical signs, perform gastric lavage after anaesthesia and intubation.
- Before the onset of clinical signs and after gastric lavage, administer activated charcoal with sorbitol as a cathartic to lessen absorption.
- Critically, control seizures with anaesthetic or anti-convulsant agents (preferably using those that do not depress respiration). Start with diazepam at 1 mg/kg with readiness to intubate. If seizures continue, pentobarbitone at 6 mg/kg IV initially and then, if necessary, by drip at 60 mg + 6 mg diazepam in 100 ml lactated Ringer's solution at a slow "to effect" continuous drip. The muscle relaxants methocarbamol or glycerol-guaiacolate can be given at 40–110 mg/kg IV to effect and later by drip. Halothane can be used as a general anaesthetic. Oxygen should always be administered.
- Give intravenous fluids containing bicarbonate (8.4% w/v) at a dose rate of 300 mg/kg and electrolytes to treat hypotension/shock, correct lactic acidosis, enhance renal excretion of 1080, and address electrolyte imbalance.
- Administer calcium gluconate at 0.2–0.5 ml/kg IV (5% solution, slowly, in fluids) to control hypocalcaemia and myocardial function.
- Antiarrhythmics such as lidocaine and procainamide will address cardiac arrhythmias.
- Maintain normal core body temperature.
- Other symptomatic treatment (such as respiratory support) can be administered as required.

- Experimental treatment of dogs with parenterally administered acetamide or bicarbonate have been detailed (Parton 2004). Administer 10 ml/kg of acetamide (using a microwave dissolve 15 g in 1 litre of 5% glucose) over 15 minutes and reduce to 8 ml/kg/hr until the litre is finished.

References

Eason, C.T.; Wickstrom, M. 2001: Sodium monofluoroacetate (1080). *In: Vertebrate pesticide toxicology manual (Poisons). Department of Conservation Technical Series 23*, Department of Conservation, Wellington, NZ. Pp. 3–21.

McLaren, J. 1999: Treatment of 1080 poisoning in dogs. *Vetscript XII. (2):3*

Osweiler, G.D. 1996: Fluoroacetate. *In: Toxicology. Williams and Wilkins, Philadelphia, USA. Pp. 291–293.*

Parton, K. 2001: Fluoroacetate-1080. *In: Veterinary clinical toxicology. Massey University, NZ. Pp. 141–153.*

Parton, K. 2004: Sodium monofluoroacetate (1080). *In: Plumlee, K.H. ed Clinical Veterinary Toxicology. Mosby, St Louis, USA. Pp. 451–454.*

Cyanide

Names and structure: Sodium cyanide, potassium cyanide, cyanide; NaCN, KCN

Commercial names of baits in NZ: Feratox, Cyanide Paste for Possum Destruction, Trappers Cyanide Paste, Cyanosil, Cyanara Ferapaste.

Appearance of formulations: Pea-sized pellets or slugs of paste coloured green. See pictures in Section 5.

Key points

- In NZ, cyanide baits are applied manually to leaves, trees or in bait stations. The toxicant in some baits may be stable in the field under cool, dry conditions for several months.
- All animals are extremely susceptible to cyanide poisoning.
- Secondary poisoning in animals that eat dead or dying animals is unlikely unless gastrointestinal tract and contents are ingested.
- As cyanide acts so quickly, there is little point in attempting to reduce absorption.
- Oxygen must be administered as soon as possible.
- Antidotal treatment exists, but must be given very shortly after ingestion of bait. Sodium thiosulphate administered IV at a dosage of 1.6 ml of a 25% solution/kg BW is best used.
- Concomitant with this, intensive supportive care is given.

Sources of poisoning

Bait

Formulation and usage. Cyanide has been used in NZ for several decades for killing possums. Baits can only be purchased and used by licensed operators. Pea-sized pieces of paste are covered with a little flour and icing sugar (or other lures such as cinnamon

or eucalyptus oil) on a rock, leaf, or stick. This paste rapidly loses its toxicity in wet conditions. The newer encapsulated cyanide pellets are more stable, more effective, and safer to use. They are placed in a possum bait station with either similar-sized cereal feed pellets or in peanut butter. Cyanide pastes contain 50–60% KCN or NaCN (500–600 mg/g), and the pellets contain 80% KCN (800 mg/g).

Availability and persistence in the environment. Cyanide in the pastes will dissipate into the environment. The stability of the cyanide is increased by the oil present in the paste bait, and by how well baits are protected from rain. Baits should not be considered safe until they are broken down and unrecognisable. Encapsulated pellets that fall from bait stations will disintegrate slowly over a period of 2–4 months.

Secondary poisoning

All animals and birds are very susceptible to cyanide poisoning, but as cyanide in dead or dying pests is found at a hazardous concentration only in the gastrointestinal tract, dogs and cats are only at risk if they ingest whole animals or the gastrointestinal tract. Practically, secondary poisoning is unlikely. There are limited data on the toxicity of cyanide to reptiles, though it would appear that cold-blooded animals such as frogs are less susceptible (LD₅₀ 60 mg/kg).

Toxicology and pathology

Toxicity

Cyanide is extremely toxic to all vertebrates, with LD₅₀ values ranging from 1 to 10 mg/kg BW (dog 5.3, cat 6). At lethal doses inhalation or ingestion of cyanide produces clinical manifestations within seconds and death invariably occurs within minutes.

Absorption, metabolism and excretion

Cyanide is rapidly absorbed through the lungs by inhalation or through the gastrointestinal tract following ingestion. It is less readily absorbed through the skin, except when the skin is cut, abraded, or moist. Free cyanide is rapidly distributed in tissue and body fluids, resulting in the very rapid onset of poisoning. Although the brain is the major target organ of cytotoxic hypoxia, cyanide concentrates in erythrocytes. The spleen may therefore contain elevated cyanide concentrations and so should be taken for

analysis in cases of suspected cyanide poisoning. In animals surviving a sublethal dose, most of the absorbed cyanide reacts with sulphane sulphur in the presence of enzymes to produce thiocyanate, which is excreted in the urine for several days afterwards. Due to this detoxification, animals can ingest sublethal doses of cyanide over extended periods without apparent harm. However, thiocyanate may accumulate in tissues, and there may be a risk of permanent brain damage in animals and humans after apparent recovery from acute or repeated exposure.

Mode of action

Cyanide disrupts energy metabolism by preventing the use of oxygen in the production of energy by means of a blockage of electron transfer from cytochrome oxidase to molecular oxygen leading to cessation of cellular respiration, so causing cellular hypoxia even in the presence of normal haemoglobin oxygenation. The brain and heart are the most seriously affected tissues. Cytotoxic hypoxia with lactate acidosis depresses the central nervous system, resulting in respiratory arrest and death. Cardiac muscle and consequent cardiac function is also severely affected.

Non-target effects

It is unlikely that domestic animals will eat cyanide baits, e.g., in trials, cats either refused to eat, or spat out cyanide bait. However, considering the very high toxicity of a bait (containing 100 mg cyanide) a bait eaten by a cat or medium-sized dog could be lethal.

Diagnosis of cyanide poisoning

Diagnosis of cyanide poisoning is based on exposure history, clinical signs (sudden death), and laboratory scrutiny and analysis.

Onset of clinical signs

Clinical manifestations may be in seconds after exposure, and death results usually in a few minutes. This often precludes veterinary help in time to give treatment.

Clinical signs

- Sudden collapse and death may be the only sign.

- More gradual signs include initial anxiety and hyperventilation, rapidly followed by generalised muscle tremor, dyspnoea, mydriasis, salivation, lacrimation, vomiting, and the voiding of faeces and urine.
- Many cardiac abnormalities (tachycardia or bradycardia, ventricular arrhythmia, atrioventricular block) may be detected. Collapse, apnoea and terminal convulsions follow due to progressive anoxia. Death can occur in as little as 5 minutes, or up to about 1 hour after exposure.
- Most animals that survive 2 hours after exposure will recover completely without treatment.
- As oxygen is not utilised in the tissues, the arterial and venous blood is bright red in colour. This may be evident in the mucous membranes, but may be obscured by pallor or even cyanosis.

Laboratory diagnosis

- The rapid onset of clinical signs, and the non-specific manifestations of anoxia together with a history of cyanide baiting will strongly suggest a toxicological aetiology. Moreover, poisoned non-target animals are usually found dead close to the source of the toxin.
- The rapid lethal course of cyanide poisoning necessitates rapid treatment, so precluding further examinations, testing or analyses.
- In a hospital setting, severe metabolic acidosis (elevated blood lactate or reduced blood pH) together with an increased anionic gap are indicative.
- In dead animals, there may be a “bitter almond” smell on close investigation of the stomach. However not everyone can smell cyanide.
- Post mortem, generalised congestion, haemorrhages in cardiac muscle and petechial haemorrhages are probably only indicative of the anoxia and convulsions.
- Hyper pink or bright red, seemingly well-oxygenated mucous membranes are highly indicative of cyanide poisoning.
- Chronic exposure to sublethal doses may lead to multiple foci of degeneration in the CNS.

- For confirmation of diagnosis, samples of stomach contents, or skeletal muscle, should be immediately frozen in airtight containers, and shipped frozen to an appropriate laboratory. Low concentrations of cyanide in tissues are indicative of intoxication.
- Whole, heparinised blood samples collected in airtight containers with no air space (submitted immediately or frozen) can also be analysed for cyanohaemoglobin or cyanide. As there is an affinity of cyanide to bind to erythrocytes, the spleen may contain elevated cyanide concentrations.

Treatment of cyanide poisoning in animals

Therapeutic goals are (1) to decrease toxin absorption before clinical signs, (2) to facilitate cyanide excretion by inducing methaemoglobinaemia (with nitrite) which preferentially binds cyanide, followed by administration of thiosulphate that is excreted with the cyanide as thiocyanate; and (3) to support respiration and cardiac function.

Recommendations for the treatment of cyanide poisoning in animals are as follows:

- If there are no clinical signs, thoroughly wash the areas around the mouth with water, and wipe dry with disposable tissues. Take care not to be exposed to remnants of the cyanide bait. Administer oxygen. If the ingestion was less than about 20 minutes previously and the animal still appears normal, induce emesis or perform careful stomach lavage under general anaesthetic. Follow with activated charcoal at 1 g/kg BW infusion to leave in the stomach.
- If there are clinical signs, immediately administer oxygen. If the diagnosis of cyanide intoxication is not certain, or in mild cases, administer 1.65 ml/kg BW of a 25% solution of sodium thiosulphate IV.
- If the cause is definitely cyanide, then also administer the otherwise toxic nitrite (which may in the absence of cyanide toxicity induce hypotension or excessive methaemoglobinaemia). Sodium nitrite at 15 mg/kg IV as a 3% solution induces methaemoglobinaemia, with the methaemoglobin binding cyanide preferentially over binding in tissues. Sodium thiosulphate at 1.25 g/kg 25% solution enables the conversion of cyanide from the cyanomethaemoglobin to thiocyanate, which is then

excreted in the urine. The treatment should be repeated at half the initial dose in 30 minutes if clinical response is insufficient.

References

Eason, C.T.; Wickstrom, M. 2001: Cyanide (Feratox). *In: Vertebrate Pesticide toxicology manual (Poisons). Department of Conservation Technical Series 23*, Department of Conservation, Wellington, NZ. Pp. 22–31.

Fitzgerald, K.T. 2001: Cyanide. *In: Peterson, M.E.; Talcott, P.A. eds Small animal toxicology*. W.B. Saunders, Philadelphia, USA. Pp. 474–480.

Gfeller, R.W.; Messonnier S.P. 2004: Cyanide. *In: Handbook of small animal toxicology and poisonings*, 2nd edition. Mosby, St Louis, Missouri, USA. Pp. 120–122.

Parton, K. 2001: Cyanide. *In: Veterinary clinical toxicology*. Massey University, NZ. Pp. 133–140.

Brodifacoum

Names and structure: Brodifacoum; 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2*H*-1-benzopyran-2-one.

Commercial names of baits in NZ: Talon, Talon 20 P, Talon Possum Bait, Pestoff Rodent Bait

Appearance of formulations: Baits are coloured blue or green and available as cereal pellet baits (waxed or unwaxed) and extruded blocks. See pictures in Section 5.

Key points

- Brodifacoum is the most commonly used second-generation anticoagulant rodenticide (SGAR) in NZ. Flocoumafen and bromadiolone are also used.
- In mainland NZ, brodifacoum baits are applied manually in bait stations against possums and rats. The toxicant in bait may be stable in the field under cool dry conditions for several months.
- Non-target mammals are all regarded as having similar susceptibility to brodifacoum poisoning. However, dogs are more likely to be poisoned than cats because of their scavenging habits.
- Secondary poisoning of an accumulative nature in animals that repeatedly eat dead or dying animals occurs, and this may manifest subacutely or chronically over weeks or months.
- Onset of signs is subacute to acute, so efforts to reduce absorption are only practical if ingestion of bait is observed or immediately suspected.
- Vitamin K₁ is an effective antidotal treatment that must be given repeatedly over many days or weeks. Daily doses of Vitamin K₁ for dogs and cats are 2.5-5.0 mg/kg given subcutaneously (SC). After the first 1-2 days, Vitamin K₁ can be administered orally.

- Parallel to this, there should be regular monitoring of coagulation activity (best with prothrombin time or PIVKA testing).
- In dogs and cats that fully recover residual long term adverse effects on animal health are possible, but unlikely.
- Animals recovering will have brodifacoum residues in the liver and so will be more sensitive to another exposure.

Sources of poisoning

Brodifacoum is currently thought to be the most widely used commensal rodenticide worldwide. It belongs to the group of second-generation anticoagulant rodenticides (SGAR) that were originally intended for use against rats resistant to warfarin (a first generation anticoagulant rodenticide, FGAR). Brodifacoum has been used successfully in many rodent eradication programmes on NZ offshore islands to protect populations of endangered indigenous birds. In addition it has been successfully used in ground-laid baits or in baits placed in bait stations to eradicate rabbits, to control wallabies and brushtail possums. Field use of brodifacoum-containing baits for rabbit or wallaby control has been discontinued in NZ. For possum control the baits are used to further reduce low possum numbers following the use of acute VP (cyanide, 1080, or cholecalciferol) for initial population reduction. The relatively delayed action of brodifacoum overcomes the problems associated with bait shyness in areas where possum control has been sustained for many years.

Bait

Formulation and usage. Only ready-to-use baits are available, containing 0.02–0.05 mg brodifacoum/g of bait material. The baits are available as blue- or green-dyed cereal-based pellets that can also be coated with wax to improve durability. Extruded block baits are also available for rodent control.

Availability and persistence in the environment. Baits may be accessible to domestic animals and, although cereal-based, may be eaten by dogs. Provided the bait is intact, brodifacoum is stable for several months at least. Cool dry conditions can ensure bait lasts for even longer. It is therefore essential that NTA do not gain access to areas

where brodifacoum is being used. When baits do break down, brodifacoum may be more easily ingested by invertebrates.

Secondary poisoning

The risk of secondary poisoning to non-target species from SGAR (e.g. brodifacoum) is considered greater than that from first-generation anticoagulant rodenticides (FGAR) (e.g. coumatetralyl), because SGAR are not substantially metabolised and excreted before death. Brodifacoum accumulates and can persist (>1 year) in the liver of sublethally poisoned wildlife or livestock. In persistence studies limited consideration has been given to organs other than the liver. This is surprising considering that quite high concentrations of anticoagulants are found in the kidneys and lungs relative to other tissues some time after dosing. The perceived hazards of secondary poisoning to non-target wildlife have prevented SGAR from being registered for field use in several countries. The risk of secondary poisoning in birds is greatest for predatory and scavenging species. Secondary poisoning of insectivorous birds has been reported in captive species feeding on insects after brodifacoum baiting.

Toxicology and pathology

Toxicity

For SGAR like brodifacoum only a single dose is needed to induce death if sufficient toxicant is ingested, and brodifacoum is extremely toxic in a number of animal species. LD₅₀ values recorded are <1 mg/kg in pigs, possums, rabbits, rats and mice, with considerable variability reported in other species, in sheep 5–25 mg/kg, in dogs 0.25–3.56 mg/kg and in cats 0.25–2.5 mg/kg. Birds are generally less susceptible. Developing foetuses may be affected – there is a report of 8 of 13 dog pups being born dead or dying soon after birth – necropsy was typical of SGAR and brodifacoum was found in the livers of 2 pups with haemorrhage. Repeated high doses caused abortions in rats, and sublethal doses have caused abortions and reduced lambing rates in sheep.

Anticoagulants are unlikely to affect invertebrates, which have different blood-clotting systems from vertebrates.

Absorption, metabolism and excretion

Brodifacoum is absorbed through the gastrointestinal tract, but is not well absorbed through the skin. After absorption, distribution is rapid and brodifacoum is bound in the liver, kidney, or pancreas in a stable form and is only excreted very slowly. Elimination from rat liver was biphasic, consisting of a rapid initial phase lasting from days 2 to 8 after dosing and a slower terminal phase when the elimination half-life was 130 days. SGAR are not readily metabolised and the major route of excretion of unbound compound is through the faeces.

Mode of action

Brodifacoum, like all other SGAR and FGAR, acts by interfering with the normal synthesis of vitamin K-dependent clotting factors in the liver of vertebrates. In the liver cells the biologically inactive vitamin K1-2,3 epoxide is reduced by the enzyme vitamin K-epoxide reductase into biologically active vitamin K, which is essential for the synthesis of prothrombin and other clotting factors (VII, IX, and X). Brodifacoum antagonism of the enzyme causes a gradual depletion of the active form of the vitamin, and consequently of vitamin K-dependent clotting factor activity (the factors are produced, but are not activated and these inactive forms are identified by PIVKA). This results in an increase in blood-clotting time until spontaneous haemorrhage occurs. The greater potency of SGAR compared to FGAR is likely to be related to their greater affinity for vitamin K-epoxide reductase and subsequent accumulation and persistence in the liver. Anticoagulants share a common binding site, but the SGAR have a greater binding affinity than the FGAR. All tissues that contain vitamin K-epoxide reductase (e.g. liver, kidney, and pancreas) are target organs for accumulating these toxicants.

Non-target effects

Lethally or sublethally poisoned pests may be debilitated and show behavioural changes (such as appearing outside burrows or in the open in the daytime), and so are much more easily caught by dogs and cats. Recent surveys of wildlife have indicated that contamination of kiwi and other protected native species has occurred in areas where brodifacoum was being correctly used. Game birds, feral pigs and feral deer that might be eaten by people have also been contaminated, so it was recommended that animals should not be hunted for human consumption from baited areas for at least 9 months after the application of the baits. Protected NZ birds most at risk from feeding directly

on brodifacoum baits are the naturally inquisitive, omnivorous species (e.g. weka, pukeko and kea). There are no published LD₅₀ data on the acute toxicity of brodifacoum to reptiles or amphibians. However, reptiles, at least, are known to be susceptible to brodifacoum. Invertebrates may ingest bait with no harm and if eaten by other animals can add to their SGAR liver burden. In a study in weta, brodifacoum persisted for approximately 1 week after dosing, so contaminated invertebrates may pose a short-lived risk of secondary poisoning to insectivorous or omnivorous animals.

Diagnosis of brodifacoum poisoning

Diagnosis of anticoagulant poisoning is based on history of exposure, clinical signs, response to treatment, laboratory analyses, and in lethal cases, necropsy lesions.

Onset of clinical signs

There is usually a lag period of 1–5 days between exposure and the onset of clinical signs, representing the time for depletion of hepatic stores of vitamin K, and reduction of preformed vitamin K-dependent clotting factor concentration in the plasma to the point of functional deficiency. In possums this may take as long as 1–4 weeks.

Clinical signs

- Initial clinical signs are usually characterised by depression/lethargy and anorexia, followed shortly by anaemia with pale mucous membranes, dyspnoea, coughing (may be with blood), exercise intolerance, and haemorrhaging from numerous sites, as evidenced by haematemesis (vomiting blood), epistaxis (blood from the nose), haemoptysis (bronchial or pulmonary bleeding), haematuria, vaginal bleeding, melena (“tarry” faeces), and SC haematomas in various locations.
- Periarticular or intra-articular haemorrhage causing swollen joints and lameness is common.
- Onset of signs may occur suddenly, even as an apparent sudden death; this is especially true when haemorrhage occurs in the brain, thorax or heart.
- Haemorrhage is often as ecchymoses and may be massive in size.

- If haemorrhage involves the brain or spinal cord, profound depression, ataxia or convulsions may occur. Animals experiencing prolonged poisoning may be icteric (jaundiced). As blood loss continues, cardiac murmurs, irregular heartbeat, weak peripheral pulses, ataxia, recumbency, dyspnoea, coughing, and coma may be observed. Disseminated intravascular coagulation (DIC) may occur in the final stages.
- Death may occur from 2 days to several weeks after exposure from multiple causes related to anaemia or hypovolaemic shock.

Laboratory diagnosis

- Laboratory evaluation of suspect anticoagulant exposures in domestic animals includes measurement of packed cell volume (haematocrit), clotting parameters, and most specifically, detection of residues (in the blood in live animals or in liver).
- The activity of vitamin K-dependent clotting factors (II, VII, IX, and X) is commonly measured using a variety of tests, including prothrombin time (PT), activated clotting time (ACT), activated partial thromboplastin time (APTT) and more recently the PIVKA (proteins induced by vitamin K antagonists) test.
- Abnormal prolongation of PT is usually the earliest indicator of anticoagulant-induced coagulopathies, due to the involvement of factor VII in the coagulation pathway assessed by this clotting parameter. Factor VII has the shortest half-life of the vitamin K-dependent factors (6.2 hours in dogs), and is therefore the first to be depleted in plasma. Elevations of PT from 2–6 times normal may occur within 24–48 hours of ingestion of a toxic dose.
- The PIVKA test may detect abnormalities even earlier, but in the case of poisoning is probably only slightly more sensitive than the other tests. This is followed several hours later by elevation in APTT to 2–4 times normal values in cases of significant exposure, indicative of factor IX depletion.
- In general, clotting parameter times are suggestive of anticoagulant exposure if they are $\geq 25\%$ longer than normal values.
- Assessment of coagulation parameters requires a sample of fresh, non-haemolysed blood collected in a sodium citrate (Blue Top) tube, stored at 4°C, and submitted as

soon as possible. The diagnostic laboratory may require submission of a parallel sample from a “normal”, unexposed animal of the same species to serve as a control.

- Anticoagulant-induced coagulopathies (clotting disorders) can best be distinguished from other types of coagulopathies by clinical response to treatment with the specific antidote, vitamin K₁. Tests used to assess coagulation time should indicate significant improvement in clotting ability within 12–24 hours of initiation of treatment, and should return to normal within 36–48 hours. A mild acidosis may be seen.
- Other blood tests have limited use in diagnosis but haematocrit and total protein testing may aid in assessing recovery.
- Radiology or ultrasound may aid in detection of massive haemorrhage, particularly in the thorax. Thoracentesis is valuable. If unclotted blood is aspirated, compare haematocrit and total protein levels with those of venous blood for diagnosis of haemothorax.
- Generalised haemorrhage is evident at post-mortem. Areas commonly affected are the lungs, the thoracic or abdominal cavities, mediastinal space, periarticular tissues, subcutaneous tissues, subdural space, and gastrointestinal tract. The heart is sometimes rounded and flaccid with subepicardial and subendocardial haemorrhages. Sudden deaths are often marked by massive haemothorax, haemopericardium, or pulmonary oedema or haemorrhage. Histopathological scrutiny of the liver may reveal centrilobular necrosis as a result of anaemia and hypoxia.

Treatment of brodifacoum poisoning in animals

Dogs and cats usually present with signs of haemorrhage or anaemia, or are asymptomatic but with a history of recent ingestion of anticoagulant bait. In the latter cases, either the dose ingested was insufficient to cause significant inhibition of vitamin K-dependent clotting factor production, or insufficient time has elapsed to deplete pre-exposure plasma clotting factor concentrations to the point of deficiency. Treatment of anticoagulant poisoning can be expensive as SGAR poisoning demands prolonged therapy, so animals presenting with a history of exposure but no clinical signs should be assessed carefully before prolonged treatment is initiated.

Therapeutic goals for veterinarians in the treatment of anticoagulant poisoning are (1) to decrease toxicant absorption; (2) to correct blood loss and/or hypovolaemia; and (3) to correct clotting factor deficiencies. Recommendations for the treatment of anticoagulant poisoning in companion animals are as follows:

If the dog or cat is presented asymptomatic, within several hours of suspected or confirmed oral exposure:

- Induce vomiting (if <3 hours) and/or perform gastric lavage.
- Administer activated charcoal (1–2 g/kg) with a saline cathartic (sodium sulphate at 250 mg/kg in 5–10 times as much water).
- Decision to initiate vitamin K₁ therapy depends on potential exposure dose and effectiveness of decontamination. If suspected dose ingested is low (<10% of LD₅₀), decontamination may suffice, with instructions for owner to observe for signs of haemorrhage. If potential exposure is more significant, measure PT at 24, 48 and 72 hours after ingestion. If results are normal, defer treatment but monitor for 10–30 days (if SGAR suspected).

If the dog or cat is presented with signs of haemorrhage and/or anaemia:

- Animals with a haematocrit of <15%, with severe bleeding, or with associated complications of anaemia, require clotting factor replacement immediately. Immediately correct low haematocrit and/or hypovolaemia, and provide clotting factors with IV transfusion using fresh or frozen plasma (5–10 ml/kg) or fresh whole blood at 10–20 ml/kg. Give the initial 25% of the volume relatively rapidly, and the remainder by slow drip.
- Handle affected animals with care and avoid self-induced trauma. Sedate as needed (avoid protein-binding drugs like promazine that may displace toxicant residues and exacerbate signs). Maintain core body temperature. Oxygen is beneficial with severe dyspnoea. Give replacement IV fluids only after clotting factors have been administered. Crystalloids are of benefit, whereas colloids (mainly dextran) are contraindicated.
- Initiate antidotal therapy using vitamin K₁, which is the only effective form available (vitamin K₃ is not to be used). Hepatic bioavailability of oral vitamin K₁ is greater than the parenteral form, so this route should be used unless contraindicated (e.g. in

cases of vomiting, gastrointestinal haemorrhage, or concurrent administration of activated charcoal). If parenteral administration is required on initial presentation, vitamin K₁ formulations can be given IV (slowly, over 15–20 minutes, with a small-bore needle), although this route is associated with frequent anaphylactic reactions. IM administration may cause haemorrhage, so is not recommended. The subcutaneous route is safer, but absorption is slow in dehydrated animals and so the dose is divided and injected into three locations, using a small-bore needle.

Recommended daily doses of vitamin K₁ for dogs and cats range from 1 mg/kg for FGAR to 2.5–5.0 mg/kg for brodifacoum. If the identity of the toxicant is not known, use the higher dose. After the first 1-2 days, the Vitamin K₁ should be administered orally. Oral bioavailability is enhanced by concurrent feeding with a teaspoon of (fatty) canned dog food.

- Oral vitamin K₁ therapy must be maintained for as long as the toxicant is active in inhibiting vitamin K epoxide recycling. Recommendations for duration of treatment in companion animals range from 3–10 days for FGAR to 30 days for brodifacoum. In all cases, premature termination of treatment should be avoided. It is best to treat for 7 days initially, then monitor treatment efficacy (with PT) 48 hours after temporarily ceasing vitamin K₁ therapy. If PT is normal, it should be rechecked 3 days later. Abnormal levels demand continuing therapy of another 2 weeks at least.
- With severe dyspnoea, massive thoracic haemorrhage may be detected by radiography and treated by drainage.
- Avoid protein-bound drugs, elective surgery, strenuous exercise, and large volumes of fatty food during the convalescent period. Previously exposed animals may be more sensitive to subsequent anticoagulant exposure for weeks to months after recovery, due to biologically active residues in the liver.
- Pregnant or lactating animals will require special attention and treatment with regard to potential toxic effects on the foetuses or young.

References

Campbell, A.; Chapman, M. 2000: Anticoagulant rodenticides. *In*: Handbook of poisoning in dogs and cats. Blackwell, UK. Pp. 64–72.

Eason, C.T.; Wickstrom, M. 2001: Anticoagulant poisons. *In: Vertebrate pesticide toxicology manual (Poisons). Department of Conservation Technical Series 23*, Department of Conservation, Wellington, NZ. Pp. 41–74.

Felice, L.J.; Murphy, M.J. 1995: CVT update: Anticoagulant rodenticides. *In: Kirk's current veterinary therapy, vol. XII Small animal practice*. W.B. Saunders, Philadelphia, USA. Pp. 228–232.

Mount, M.E. 1998: Proteins induced by vitamin K ascence or antagonists (“PIVKA”). *In: Kirk's current veterinary therapy, vol. IX Small animal practice*. W.B. Saunders, Philadelphia, USA. Pp. 513–515.

Murphy, M.J.; Talcott, P.A. 2001: Anticoagulant rodenticides. *In: Peterson, M.E.; Talcott, P.A. eds Small animal toxicology*, W.B. Saunders, Philadelphia, USA. Pp. 406–419.

Murphy, M.J. 2002: Rodenticides. *In: The veterinary clinics of North America: small animal practice*. W.B. Saunders, Philadelphia, USA. Pp. 469–484.

Osweiler, G.D. 1996: Anticoagulants. *In: Toxicology*. Williams and Wilkins, Philadelphia, USA. Pp. 276–279.

Parton, K. 2001: Anticoagulant rodenticides. *In: Veterinary clinical toxicology*. Massey University, NZ. Pp. 120–128.

Robben, J.H.; Kuijpers, E.A.P.; Mout, H.C.A. 1998: Plasma superwarfarin levels and vitamin K1 treatment in dogs with anticoagulant rodenticide poisoning. *Veterinary Quarterly 20*: 24–27.

Other second-generation anticoagulant rodenticides

Flocoumafen

Name and structure: Flocoumafen; 4-hydroxy-3-[1,2,3,4-tetrahydro-3-[4-(4-trifluoromethylbenzyloxy)phenyl]-1-naphthyl] coumarin

Commercial name of bait in NZ: Storm

Appearance of formulations: Baits are coloured blue and are available as cereal pellet baits. The bait contains 50 mg flocoumafen/kg of bait material.

Key points

- In NZ, flocoumafen is a rodenticide not used extensively. Ready-made baits are used against commensal rodents. The toxicant is probably stable in bait in the field under cool dry conditions for several months.
- Non-target mammals are all regarded as having similar susceptibility to flocoumafen poisoning.
- Flocoumafen is very similar to brodifacoum with regard to toxicity, diagnosis and treatment.

Bromadiolone

Name and structure: Bromadiolone; 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxy-2*H*-1-benzopyran-2-one.

Commercial names of baits in NZ: Rid Rat Super Wax Baits, Bromatrol, Bromard, Super Squeak

Appearance of formulations: Baits are coloured blue or green and available as waxed grain-based baits and extruded blocks. See pictures in Section 5. All the baits contain 50 mg bromadiolone/kg of bait material.

Key points

- In NZ, bromadiolone is a rodenticide not used extensively. Ready-made baits are used against commensal rodents. The toxicant is probably stable in bait in the field under cool dry conditions for several months.
- Non-target mammals are all regarded as having similar susceptibility to bromadiolone poisoning.
- There may be a lower risk of secondary poisoning compared to brodifacoum because it is less potent.
- Bromadiolone is very similar to brodifacoum with regard to toxicity, diagnosis and treatment.

Difethalione

Name and structure: Difethalione; 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2*H*-1-benzothiopyran-2-one

Commercial name of bait in NZ: Baraki Rodenticide Pellets, Baraki Rodenticide Wax Block

Appearance of formulations: The grain bait and the wax block both contain 25mg difethalione/kg of bait material.

Key points

- In NZ, difethalione is a rodenticide not used extensively. Ready-made baits are used against commensal rodents. The toxicant is probably stable in bait in the field under cool dry conditions for several months.
- Non-target mammals are all regarded as having similar susceptibility to difethalione poisoning.
- Difethalione is very similar to brodifacoum with regard to toxicity, diagnosis and treatment.

Pindone

Name and structure: Pindone; 2-(2,2-dimethyl-1-oxopropyl)-1H-indene-1,3(2*H*)-dione

Commercial name of bait in NZ: Pindone Rabbit Pellets, Pindone Possum Pellets, Pindone RS5 Rabbit Pellets (also Pindone Liquid Concentrate containing 3.4% pindone).

Appearance of formulations: Baits are coloured green and are available as cereal-based pellets.

Key points

- Pindone is one of the three first-generation anticoagulant rodenticides (FGAR) used in NZ. As FGAR are less toxic than SGAR, concentrated powders and solutions are sold to pest control officers to make their own baits.
- Pindone has been much used in NZ against rabbits and less effectively against possums. The toxicant is probably stable in bait in the field under cool dry conditions for at least several weeks.
- The toxicity and non-target impacts of pindone are poorly documented, but are lower than SGAR.
- Non-target mammals are regarded as having low susceptibility to pindone poisoning under normal use conditions. However, susceptibility in mammals and birds is increased by multiple exposures to FGAR.
- Secondary poisoning in animals that repeatedly eat dead or dying animals is unlikely.
- Onset of signs is slow, so there is little point in trying to reduce absorption.
- There is an excellent antidotal treatment, vitamin K₁, which must be given repeatedly over several days as for SGAR poisoning.
- Parallel to this, there should be regular monitoring of coagulation activity to ensure that there was no SGAR exposure.

- It is possible but unlikely that there will be any deleterious pathological changes in recovered animals that endanger their future health.

Sources of poisoning

Pindone belongs to the group of the first-generation anticoagulant rodenticides (FGAR) that have been largely supplanted by the SGAR. Pindone is currently registered in NZ for the control of rabbits and possums, and is most effective for rabbit control.

Bait

Formulation and usage. Three ready-to-use baits are available, containing 0.25–0.5 mg pindone/kg of bait material. A concentrated liquid solution containing 34g pindone/litre may be used by pest control officers to make up baits. On mainland NZ cereal baits are used in bait stations.

Availability and persistence in the environment. Limited data indicate that pindone is relatively slowly leached from baits. It is therefore probably stable in the environment for a reasonable length of time.

Secondary poisoning

The risk of secondary poisoning of NTA with FGAR is minor compared with SGAR, due to lack of accumulation of residues and much lower persistence times.

Toxicology and pathology

Toxicity

For FGAR such as pindone, either very large single doses (a highly improbable occurrence with baits) or repeated smaller doses are generally needed to cause poisoning and death. Although acute LD₅₀ are therefore not practical indicators of the likelihood of poisoning, limited data record LD₅₀ to be 6–18 mg/kg in rabbits, 50 in dogs, 75–100 in rats, ~100 in sheep and >100 in possums. In a repeated-dose study, cattle and cats were more susceptible than dogs, chickens and sheep, with horses being

the least susceptible. The rabbit remains outstanding as the most susceptible mammalian species evaluated to date.

Absorption, metabolism, and excretion

Pindone is absorbed through the gastrointestinal tract. Plasma concentrations in dogs remain higher than liver concentrations. Faster excretion causes pindone to be far less persistent than the SGAR, with liver residues persisting for several days rather than months.

Mode of action

All the FGAR act like the other anticoagulant toxicants by interfering with the normal synthesis of vitamin K-dependent clotting factors in the liver. Repeated dosing is needed as the toxicant is excreted relatively rapidly and several days of exposure are needed to sufficiently depress coagulation function.

Non-target effects

No systematic studies have been conducted to determine the non-target effects of pindone. Field data indicate occasional extensive bird kills; even less is known about the effects on invertebrates and reptiles. There are anecdotal reports that raptors are particularly susceptible to secondary poisoning.

Diagnosis of pindone poisoning

As for SGAR, the diagnosis of FGAR poisoning is based on exposure history, clinical signs, response to treatment, laboratory analyses, and in lethal cases, lesions.

Onset of clinical signs

After ingestion of toxicant for several days, there is usually a delay of 3–7 days before the onset of clinical signs.

Clinical signs

Clinical signs reflect some manifestations of haemorrhage, and are similar to those detailed for brodifacoum.

Laboratory diagnosis

- As for SGAR, laboratory evaluation of suspect FGAR exposures includes measurement of haematocrit, clotting parameters, and residue analyses.
- Assessment of coagulation parameters requires a sample of fresh, non-haemolysed blood collected in a sodium citrate (Blue Top) tube, stored at 4°C, and submitted as soon as possible. The diagnostic laboratory may require submission of a parallel sample from a “normal”, unexposed animal of the same species to serve as a control.

Treatment of pindone poisoning in animals

Treatment of FGAR poisoning is in principle exactly the same as for SGAR, but the duration of vitamin K administration is much less, only several days.

References

As for brodifacoum

Other first-generation anticoagulant rodenticides

Coumatetralyl

Name and structure: Coumatetralyl; 4-hydroxy-3-(1,2,3,4-tetrahydro-1-naphthyl) coumarin

Commercial name of baits in NZ: Racumin, Racumin Mouse and Rat Blocks, Racumin Paste, No Rats & Mice, Tracks No Rats & Mice

Appearance of formulations: Baits are coloured blue. See pictures in Section 5.

Key points

- Coumatetralyl is one of the three FGAR used in NZ. As FGAR are less toxic than SGAR, formulations can be sold to the general public.
- Coumatetralyl has been used in NZ only against rodents, though a possum bait is currently (2004) being investigated. The toxicant is probably stable in the field bait under cool dry conditions for at least several weeks.
- The toxicity and non-target impacts of coumatetralyl are much less than the SGAR.
- Non-target mammals are regarded as having low susceptibility to coumatetralyl poisoning under normal use conditions.
- Secondary poisoning in animals that repeatedly eat dead or dying animals is unlikely.
- Onset of signs is slow, so there is little point in trying to reduce absorption.
- There is an excellent antidotal treatment, vitamin K₁, that must be given repeatedly over several days
- Parallel to this, there should be regular monitoring of coagulation activity (prothrombin time) to ensure that there was no SGAR exposure.
- It is possible but unlikely that there will be any deleterious pathological changes in recovered animals that endanger their future health.

Sources of poisoning

Coumatetralyl is one of the three FGAR used in NZ, that have been largely supplanted by the SGAR. Coumatetralyl is currently registered in NZ for the control of rodents.

Bait

Formulation and usage. Three baits are available, containing 370–500 mg coumatetralyl/kg of bait material. A tracking powder contains 7.4 g coumatetralyl/kg, and a paste contains 375 mg coumatetralyl/kg.

Availability and persistence in the environment. Limited data indicate that coumatetralyl is probably stable in the environment for at least several weeks.

Secondary poisoning

The risk of secondary poisoning with FGAR to non-target species is minor compared with SGAR, due to lack of accumulation of residues.

Toxicology and pathology

Toxicity

For FGAR such as coumatetralyl, either very large single doses (a highly improbable occurrence with baits) or repeated smaller doses are needed to cause poisoning and death.

Absorption, metabolism, and excretion

Faster excretion causes coumatetralyl to be far less persistent than the SGAR.

Mode of action

All the FGAR act similarly by interfering with the normal synthesis of vitamin K-dependent clotting factors in the liver. Repeated dosing is needed as the toxicant is excreted relatively rapidly and several days of exposure are needed to sufficiently depress coagulation function.

Non-target effects

No systematic studies have been conducted to determine the non-target effects of coumatetralyl.

Diagnosis of coumatetralyl poisoning

As for SGAR, the diagnosis of FGAR poisoning is based on exposure history, clinical signs, response to treatment, laboratory analyses, and in lethal cases, lesions.

Onset of clinical signs

After ingestion of toxicant for several days, there is usually a delay of 3–7 days before the onset of clinical signs.

Clinical signs

Clinical signs reflect some manifestations of haemorrhage, and are similar to those described for brodifacoum.

Laboratory diagnosis

- Laboratory evaluation of suspect FGAR exposures includes measurement of haematocrit, clotting parameters, and residue analyses, as for SGAR.
- Assessment of coagulation parameters requires a sample of fresh, non-haemolysed blood collected in a sodium citrate (Blue Top) tube, stored at 4°C, and submitted as soon as possible. The diagnostic laboratory may require submission of a parallel sample from a “normal”, unexposed animal of the same species to serve as a control.

Treatment of coumatetralyl poisoning in animals

Treatment of FGAR poisoning is in principle exactly the same as for SGAR, but the duration of vitamin K administration is much less, only several days.

References

As for brodifacoum.

Diphacinone

Name and structure: Diphacinone; 2-diphenylacetyl-1,3-indandione

Commercial name of baits in NZ: Pest Gone Rodent Bait, Ditrac All-weather Rodent Block, Pestoff Ferret Paste

Appearance of formulations: Baits are coloured green. See pictures in Section 5.

Key points

- Diphacinone is one of the three FGAR used in NZ. As FGAR are less toxic than SGAR, formulations can be sold to the general public.
- Diphacinone has been used in NZ against rodents and ferrets. The toxicant is probably stable in the field bait under cool dry conditions for at least several weeks.
- The toxicity and non-target impacts of diphacinone are much less than the SGAR
- Non-target mammals are regarded as having low susceptibility to diphacinone poisoning under normal use conditions.
- Secondary poisoning in animals that repeatedly eat dead or dying animals is unlikely.
- Onset of signs is slow, so there is little point in trying to reduce absorption.
- There is an excellent antidotal treatment, vitamin K₁, that must be given repeatedly over several days
- Parallel to this, there should be regular monitoring of coagulation activity (prothrombin time) to ensure that there was no SGAR exposure.
- It is possible but unlikely that there will be any deleterious pathological changes in recovered animals that endanger their future health.

Sources of poisoning

Diphacinone is one of the three FGAR used in NZ, that have been largely supplanted by the SGAR.

Bait

Formulation and usage. The grain bait and wax block both contain 50 mg diphacinone/kg of bait material, and the paste contains 300 mg diphacinone/kg. On mainland NZ cereal baits are used in bait stations. Formulations are used against rodents and ferrets.

Availability and persistence in the environment. Limited data indicate that diphacinone is probably stable in the environment for at least several weeks.

Secondary poisoning

Diphacinone is more persistent than pindone or coumatetralyl and may be more of a risk for secondary poisoning, but still much less than with SGAR.

Toxicology and pathology

Toxicity

For FGAR such as diphacinone, either very large single doses (a highly improbable occurrence with baits) or repeated smaller doses are generally needed to cause poisoning and death. The more toxic ferret paste is the more hazardous.

Absorption, metabolism, and excretion

Faster excretion causes diphacinone to be far less persistent than the SGAR. Accumulation is mainly in the liver and less in the kidney and lungs, with least in the muscle, brain and fat.

Mode of action

All the FGAR act like the other anticoagulant toxicants by interfering with the normal synthesis of vitamin K-dependent clotting factors in the liver. Repeated dosing is needed as the toxicant is excreted relatively rapidly and several days of exposure are needed to sufficiently depress coagulation function.

Non-target effects

No systematic studies have been conducted to determine the non-target effects of diphacinone.

Diagnosis of diphacinone poisoning

As for SGAR, the diagnosis of FGAR poisoning is based on exposure history, clinical signs, response to treatment, laboratory analyses, and in lethal cases, lesions.

Onset of clinical signs

After ingestion of toxicant for several days, there is usually a delay of 3–7 days before the onset of clinical signs.

Clinical signs

Clinical signs reflect some manifestations of haemorrhage, and are similar to those described for brodifacoum.

Laboratory diagnosis

- Laboratory evaluation of suspect FGAR exposures includes measurement of haematocrit, clotting parameters, and residue analyses, as for SGAR.
- Assessment of coagulation parameters requires a sample of fresh, non-haemolysed blood collected in a sodium citrate (Blue Top) tube, stored at 4°C, and submitted as soon as possible. The diagnostic laboratory may require submission of a parallel sample from a “normal”, unexposed animal of the same species to serve as a control.

Treatment of diphacinone poisoning in animals

Treatment of FGAR poisoning is in principle exactly the same as for SGAR, but the duration of vitamin K administration is much less, only several days.

References

As for brodifacoum

Cholecalciferol

Names and structure: Cholecalciferol, vitamin D₃; 9,10-secocholesta-5,7,10 (19)-trien-3-ol

Commercial name of baits in NZ: Feracol

Appearance of formulations: Bait is coloured green and are available as cereal block baits, paste, or gel baits.

Key points

- Cholecalciferol has been used in NZ against possums and to a lesser extent against rodents. The toxicant is probably stable in a protected paste formulation for at least several weeks.
- Non-target mammals are regarded as having low susceptibility to cholecalciferol poisoning under normal use conditions.
- Secondary poisoning in animals that repeatedly eat dead or dying animals is unlikely, but dogs could be affected in cases of extreme exposure.
- Onset of signs is slow, so once signs appear, there is little point in trying to reduce absorption. However, if very recent ingestion is suspected, administer activated charcoal (1-2 g/kg) with a cathartic, repeated doses are given over 2 days.
- There is no antidotal treatment, so treatment of clinical cases is based on efforts to reduce blood calcium levels – diuresis induced with IV saline and furosemide, and corticosteroid administration.
- Supportive treatment is intensive, accompanied by repeated blood calcium monitoring.
- Cholecalciferol induces marked pathological changes, so treatment of severe toxicoses is not usually effective.
- There may be deleterious pathological changes in recovered animals that could endanger their future health.

Sources of poisoning

Vitamin D naturally exists in two forms, vitamin D₃ (cholecalciferol) and vitamin D₂ (ergocalciferol), both forms appearing to be identically metabolised and with similar biological activity in mammalian species. Cholecalciferol is more readily available and less expensive than ergocalciferol and therefore became the marketed toxicant. Dogs may also ingest vitamin D human medications.

Bait

Formulation and usage. The paste contains 8 g cholecalciferol/kg. It is used against possums and rodents in bait stations.

Availability and persistence in the environment. Cholecalciferol may be degraded by sunlight or oxidised and inactivated by moist air within a few days, but the paste has been specifically formulated to be stable in the environment, probably for at least several weeks. Cholecalciferol is stable in the environment in paste and baits for at least 12 and 26 months respectively.

Secondary poisoning

Cholecalciferol is considered to pose a relatively low risk of secondary poisoning - secondary exposure could occur in animals eating gastro-intestinal contents of prey very recently exposed to the toxicant. Cats and dogs were fed poisoned possums with no deleterious effect in cats but with moderate poisoning in dogs fed 5 carcasses.

Toxicology and pathology

Toxicity

Possums and rabbits are most sensitive, with rodents and dogs having intermediate sensitivity and ducks being relatively resistant. The LD₅₀ in the rabbit was 9 mg / kg BW, in possums 17, in rodents 43, in dogs 85, cats 50–200 and in ducks 2000. However, clinical reports indicate that doses of as low as 0.5–5 mg/kg can be toxic to dogs, and that doses of 2–20 mg/kg are fatal, especially in small breeds and young animals. Some data suggest a higher LD₅₀ in cats, others indicate that they may be even

more sensitive than dogs, repeated exposure has an accumulative effect. Animals with renal disease or on a high calcium diet are most at risk.

Absorption, metabolism, and excretion

Cholecalciferol is well absorbed from the intestines and is metabolised in the liver to 25-hydroxycholecalciferol (25OHD). 25OHD is converted in the kidney to 24,25-dihydroxycholecalciferol and 1,25-dihydroxycholecalciferol. The latter metabolite is the most biologically active form of the vitamin, and has a functional half-life of about 3 days in the blood. 25OHD may persist for weeks in possums, but is probably partially degraded after ingestion by mammalian predators, so reducing risk. The half-life of cholecalciferol and 25OHD in animals may be up to 30 days with toxic effects lasting weeks. Excretion is about 70% through the bile into the intestines (with recycling) and 30% in the urine.

Mode of action

In order to gain biological and toxicological activity, cholecalciferol must undergo metabolic conversion to 25OHD, which increases calcium absorption from the gastrointestinal tract, mobilises calcium stores from bones into the bloodstream, and decreases calcium excretion by the kidneys. The net result is elevated concentrations of blood calcium (hypercalcaemia), and calcification of tissues in the cardiovascular system, kidneys, stomach, lungs, and muscles. Mineralisation and blockage of blood vessels appears to be the mode of action of cholecalciferol in the possum and rodents, with death probably from heart failure. In other species, including cats and dogs, renal failure (caused by vessel blockage and nephrocalcinosis) and gastrointestinal haemorrhage appear more prominently.

Non-target effects

Because vitamin D₃ is a naturally occurring essential vitamin, there may be a tendency to consider baits containing cholecalciferol as safe to NTA. However, all bait containing cholecalciferol must be treated as potentially poisonous to NTA, and must be handled and dispensed as carefully as other types of toxic bait. Despite the low toxicity of cholecalciferol to ducks, there are data that indicate that some avian species may be more sensitive to poisoning.

Diagnosis of cholecalciferol poisoning

The diagnosis of cholecalciferol poisoning is based on exposure history, clinical signs, the finding of hypercalcaemia, laboratory analyses, and in lethal cases, pathological lesions.

Onset of clinical signs

The occurrence, speed of onset, and severity of signs is dose-dependent. Signs of poisoning in dogs and cats usually begin 12–48 hours after exposure, more often in the later time frame.

Clinical signs

- Initial clinical signs may be non-specific and moderate, and include anorexia, depression, constipation and weakness.
- Manifestations become more severe 24–36 hours after onset as serum calcium levels increase, and they may start with polydipsia, and then repeated vomiting, polyuria, dehydration, sometimes diarrhoea, and rarely seizures.
- Haematesis and melena (“tarry” faeces) may indicate severe ulceration.
- Renal effects, including polyuria, hyposthenuria and azotaemia (increased blood urea and creatinine levels) become more pronounced, and depression deepens.
- Hypercalcaemia causes a transient calciuria, and cardiac effects including bradycardia and ventricular arrhythmias or fibrillation can be marked.
- Death usually occurs in 2–5 days from the onset of clinical signs. Cause of death is probably mainly due to cardiac failure and shock.

Laboratory diagnosis

- The most significant and specific clinical pathology alteration is hypercalcaemia. Total serum calcium concentration begins to increase about 24 hours after exposure, and values of >12.5 mg/dl in adult dogs (normal 9.5–12.0) or >13.5 in growing dogs are highly suggestive of cholecalciferol poisoning; levels of >16 mg/dl are common.
- Elevations of serum phosphorus (from <5.5 mg/dl to >8.0) may precede hypercalcaemia by 12 hours, and may serve as a non-specific indicator of exposure.

- Renal azotaemia (urea >25 mg/dl) and hyposthenuria (urine specific gravity in the 1.002–1.006 range) are common, and proteinuria and glucosuria may be seen in some acute cases. Calcium concentrations in the kidney cortex may reach 3000 ppm (wet weight) in poisoned animals, compared with about 50–200 ppm in normal dogs.
- A more specific test is the calcium:phosphorus ratio in the kidney cortex, where values of 0.4–0.7 are diagnostic (normal <0.1). Of the specific toxic compounds, increased serum concentrations of 1, 25-dihydroxycholecalciferol or 25OHD are the most practical and sensitive indicators.
- The main gross pathological lesion seen in dogs and cats is often haemorrhagic gastroenteritis.
- Other signs are pale enlarged kidneys with congested cortical vessels, pallid heart musculature and petechial haemorrhages in various tissues; at a later stage, pale, mineralised streaks may be seen on renal cortical surfaces.
- Histopathology shows degeneration, necrosis and widespread calcification particularly of renal tubules, submucosal and mucosal regions of stomach and small intestine, heart, and arterial walls of viscera (and in other tissues). Radiography or ultrasonography may reveal mineralisation in the kidneys and elsewhere.

Treatment of cholecalciferol poisoning in animals

Treatment of animals presented with severe clinical signs is urgent, and yet difficult and prolonged, as hypercalcaemia is present, and the prognosis is poor. Treatment should be initiated rapidly. Therapeutic goals are (1) to decrease cholecalciferol absorption; (2) to correct fluid and electrolyte imbalances; and (3) to prevent or reduce hypercalcaemia. A recommended protocol is as follows (treatment should be followed in order):

- Determine baseline serum calcium as soon as the animal is presented, and continue to monitor every 24 hours for at least 6 days.
- If ingestion was recent (<3 hours), induce emesis, or perform gastric lavage.
- In all cases, administer activated charcoal (1–2 g/kg) with a cathartic.

- Continue activated charcoal (at 0.5–1.0 g/kg t.i.d.) for 1–2 days to reduce enterohepatic recirculation of vitamin D and its active metabolites.
- Monitor blood urea and creatinine, urine specific gravity, and ECG parameters, beginning 24 hours after exposure.
- A low calcium diet should be offered for 2–3 weeks and vitamin D avoided.

Hypercalcaemia is treated with:

- Prompt (within the first 24 hours) diuresis to increase excretion using IV normal saline and furosemide (5 mg/kg initial IV bolus, followed by 3–4 mg/kg orally t.i.d.) to help enhance renal calcium excretion. Thiazide diuretics are contraindicated since they may decrease urinary calcium.
- Corticosteroid administration (prednisolone at 2–4 mg/kg, divided, b.i.d., IM or SC) inhibits the release of osteoclast-activating factors, reduces intestinal calcium absorption, and promotes renal calcium excretion.
- If serum calcium is >14 mg/dl, or hypercalcaemia is prolonged and unresponsive, calcitonin may be administered at a dosage of 4–6 IU/kg SC or IM every 2–3 hours initially to inhibit osteoclast activity, until serum calcium levels stabilise (dosage may be increased to 10–20 IU/kg if needed). Long-term administration (2–3 weeks) at increased doses may be required, as some animals become refractory to treatment. However, as some animals may react with emesis, anorexia or anaphylaxis, therapy is prolonged and costly, and efficacy has not been proven, this should not be the sole, primary treatment.
- Treatment with diuretics (furosemide at 2–4 mg/kg PO b.i.d.) and corticosteroids (prednisone at 2–4 mg/kg divided b.i.d.) should continue until serum calcium concentrations stabilise in the normal range (but monitor for hypokalaemia if treatment prolonged). It is also valuable to continue to monitor blood urea nitrogen as an indicator of renal function. Often treatment is administered for 2–4 weeks, followed by withdrawal of therapy, and retesting serum calcium after 24 hours. Continue treatment until serum calcium remains normal at 24, 48, and 72 hours after withdrawal.
- Supportive therapy must ensure proper hydration. Continuing gastrointestinal irritation may indicate anti-emetic medication (metoclopramide at 0.2–0.5 mg/kg IM

or slow IV), and treatment for gastrointestinal ulceration (liquid antacids, and sucralfate orally at 1g t.i.d.). Severely hypercalcaemic or uraemic animals may also benefit from peritoneal dialysis with calcium-free dialysate solutions.

- Life-threatening hypercalcaemia (>20 mg/dl) may be treated with IV sodium EDTA at 25–75 mg/kg/h (human doses), although EDTA is potentially nephrotoxic. A largely experimental treatment has been with the inhibitor of bone resorption, pamidronate disodium (Aredia), given early in the poisoning in a slow saline IV infusion at 1–2 mg/kg; however, this drug may be nephrotoxic and so should not be given if serum creatinine is elevated.

References

Campbell, A.; Chapman, M. 2000: Calciferol/vitamin D₂ and cholecalciferol/vitamin D₃. *In: Handbook of poisoning in dogs and cats.* Blackwell, UK. Pp. 89–96.

Dorman, D.C.; Beasley, V.R. 1989: Diagnosis and therapy for cholecalciferol toxicosis. *In: Kirk's current veterinary therapy, Vol XII, Small animal practice.* W.B. Saunders, Philadelphia, USA. Pp. 148–152.

Eason, C.T.; Wickstrom, M. 2001: Cholecalciferol. *In: Vertebrate pesticide toxicology manual (Poisons). Department of Conservation Technical Series 23,* Department of Conservation, Wellington, NZ. Pp. 32–40.

Gfeller, R.W.; Messonnier, S.P. 1998: Vitamin D rodenticides. *In: Handbook of small animal toxicology and poisonings, 2nd edition.* Mosby, St Louis, Missouri, USA. Pp. 255–258.

Gwaltney-Brant, S.M.; Rumbeiha, W.K. 2002: Newer antidotal therapies. *In: The veterinary clinics of North America: small animal practice.* W.B. Saunders, Philadelphia, USA. Pp. 323–339.

Osweiler, G.D. 1996: Rodenticides. *In: Toxicology, The National Veterinary Medical Series.* Williams and Wilkins, Philadelphia, USA. Pp. 279–282.

Parton, K. 2001: Cholecalciferol toxicity (vitamin D₃). *In: Veterinary clinical toxicology.* Massey University, NZ. Pp. 129–132.

Rumbeiha, W.K. 2001: Cholecalciferol. *In*: Peterson, M.E.; Talcott, P.A. *eds* Small animal toxicology. W.B. Saunders, Philadelphia, USA. Pp. 452–465.

Phosphorus

Names and structure: Phosphorus, yellow phosphorus; P₄

Commercial name of baits in NZ: Phosphorised Rabbit Paste, Phosphorised Possum Paste Double Strength.

Appearance of formulations: Baits are coloured green. See pictures in Section 5.

Key points

- Phosphorus is formulated as a paste that is available only to licensed operators.
- Phosphorus is an acute-acting, non-specific toxicant with no effective treatment. The toxicant is probably stable in the specially formulated paste for at least several weeks.
- Non-target mammals are regarded as having equal susceptibility to phosphorus poisoning under normal use conditions.
- Secondary poisoning in animals that eat stomach of dead or dying animals is possible, particularly with dogs and birds.
- Onset of signs is acute, so once signs appear, efforts must be made to reduce absorption. Activated charcoal (at 0.5-1.0 g/kg t.i.d) should be given.
- Orally administer 0.1% potassium permanganate (50 ml), or 1% copper sulphate (10-60 ml), or 2% hydrogen peroxide to attempt to convert the phosphorus to harmless phosphate.
- Treat shock and hypothermia.
- The liver is the main organ affected.
- There is no antidotal treatment.
- Phosphorus induces pathological changes, so it is possible that there will be changes in recovered animals that could endanger their future health.

Sources of poisoning

Phosphorus is used as a paste formulated for stability and is generally applied to turf spits on the ground. It is only available to licensed operators and is still used for rabbit and possum control by regional councils.

Bait

Formulation and usage. The rabbit paste contains 4.5 g phosphorus/kg, whereas the possum paste contains 9.5 g phosphorus/kg.

Availability and persistence in the environment. The phosphorus in the paste will probably be stable in the environment for about 3 weeks.

Secondary poisoning

Phosphorus is only likely to cause secondary poisoning in animals eating the gastrointestinal tract of prey very recently exposed to the toxicant. This is not common, but has been seen in dogs.

Toxicology and pathology

Toxicity

The sparse data available show that all species have similar sensitivity. The LD₅₀ in dogs is 2 mg/kg.

Absorption, metabolism, and excretion

Phosphorus is readily absorbed from the gastrointestinal tract and is excreted in the urine and expired air, but its pharmacokinetics have not been well studied.

Mode of action

Phosphorus is a protoplasmic (cell) toxicant, with a powerful necrotising effect in the stomach once ingested. It is mainly hepatotoxic, but it is difficult to assign the fatty degeneration seen in the kidney, brain, and heart as a primary effect or due to the effect of anoxia on those organs caused by the marked peripheral vascular dilatation induced. Hypoglycaemia, azotaemia, inhibition of glycogen formation in the liver, and many other biochemical and pathological disorders are also evident. There may be direct

cardiotoxicity, and severe delayed hepatotoxicity is seen in animals 2–4 days after ingestion.

Non-target effects

Phosphorus is a non-specific toxicant and so all animals consuming the paste are at risk. Factors affecting the risk of poisoning are disposition of bait, presence of NTA, eating behaviour of the NTA and weight of the animal eating the bait.

Diagnosis of phosphorus poisoning

The diagnosis of phosphorus poisoning is difficult, as signs are not specific and laboratory tests do not easily identify this type of poisoning. Only analysis of vomit or stomach content can specifically determine phosphorus poisoning.

Onset of clinical signs

The occurrence, speed of onset, and severity of signs is dose-dependent. Lethal doses induce severe signs within several hours.

Clinical signs

Phosphorus poisoning has been categorized into three phases:

- An acute initial phase occurring from 1–3 hours after ingestion characterised by severe recurring emesis, intense abdominal pain and (often haemorrhagic) diarrhoea. If the dosage is sufficiently high, cyanosis, severe shock, and coma may develop, with death occurring within 72 hours.
- At lower doses, an interim phase with apparent recovery occurs approximately 48 hours to several days after initial clinical signs. The breath of animals may have a garlic-like smell.
- The third stage is characterised by a recurrence of marked clinical signs, and jaundice. Death is usually due to liver necrosis and heart failure. There may be a delay of up to 3 weeks after ingestion before convulsions, coma, and death occurs.

Laboratory diagnosis

- The finding of free phosphorus in vomit, stomach contents, faeces or liver is the best diagnostic criterion.

- Non-specific indicators of liver damage in the blood and hypoglycaemia may also be present.
- If death is very sudden, inflammation, and even perforation, of the oesophagus and stomach may be the only lesions seen.
- In less acute cases that result in mortality, severe gastroenteritis, enlarged fatty liver, jaundice, and congested kidneys with petechial haemorrhages are seen. There may be subcutaneous or intramuscular extravasation of blood, and blood in the large intestine.
- There may be a garlic-like smell in the vomit, or stomach or gut content. Pathological changes are haemorrhagic gastroenteritis and fatty degeneration and necrosis of liver and kidney.

Treatment of phosphorus poisoning

There is no antidote to phosphorus poisoning, so treatment is mainly supportive and symptomatic after efforts to reduce absorption.

- Activated charcoal (at 0.5-1.0 g/kg t.i.d) should be given.
- Orally administer 0.1% potassium permanganate (50 ml), or 1% copper sulphate (10–60 ml), or 2% hydrogen peroxide to convert the phosphorus to harmless phosphate.
- Mineral oil, which solubilises phosphorus and prevents absorption, can be given.
- If ingestion was recent (< 1 hour), emesis or gastric lavage may be performed, but the potential corrosive effects of phosphorus should be considered.
- Treat shock and hypovolaemia.
- Treat for severe gastrointestis or ulceration (liquid antacids, and sucralfate orally at 1g t.i.d.).
- Give supportive liver therapy with vitamin K₁, B vitamins and a special dietary regimen.

References

Eason, C.T.; Wickstrom, M. 2001: Phosphorus. *In: Vertebrate pesticide toxicology manual (Poisons). Department of Conservation Technical Series 23*, Department of Conservation, Wellington, NZ. Pp. 87–90.

Osweiler, G.D. 1996: Yellow phosphorus. *In: Toxicology*. Williams and Wilkins, Philadelphia, USA. Pp. 288–289.

Parton, K. 2001; Phosphorus. *In: Veterinary clinical toxicology*. Massey University, NZ. Pp. 82–85.

Zinc phosphide

Names and structure: Zinc phosphide; Zn_3P_2 .

Commercial name of baits in NZ: The toxicant is in the process of being registered in NZ.

Key points

- Although zinc phosphide is not registered in NZ, it may be used in the future for possum control.
- Zinc phosphide is an acute-acting, non-specific toxicant with no specific effective treatment. The toxicant is usually less stable in the environment than other VP.
- Non-target mammals are regarded as having equal high susceptibility to zinc phosphide poisoning under normal use conditions.
- Secondary poisoning in animals that eat stomach contents of dead or dying animals is possible.
- Onset of signs is acute, so once signs appear, efforts must be made to reduce absorption.
- Signs are largely non-specific, mainly vomiting, pain, and depression.
- There is no antidotal treatment.
- Zinc phosphide induces pathological changes, so it is possible that there will be changes in recovered animals that could endanger their future health.

Sources of poisoning

Zinc phosphide is used internationally against rodents and mammalian pests in agriculture.

Bait

Formulation and usage. In other countries zinc phosphide is usually used as a rodenticide as 0.5–10% in baits, pastes or tracking powders. Phosphides are also used as insecticidal grain fumigants.

Availability and persistence in the environment. Most preparations are unstable and break down in several days in a wet or humid environment.

Secondary poisoning

Zinc phosphide is only likely to cause secondary poisoning in animals eating the gastrointestinal tract of prey very recently exposed to the toxicant. This is uncommon, but has been seen in dogs. However, there was no mortality in dogs fed minced viscera and meat from lethally poisoned possums (unpub. data).

Toxicology

Toxicity

The rapidity of phosphine release is an important determinant of toxicity, and this is enhanced by low stomach pH. All species are sensitive, although birds are probably the most sensitive. The LD₅₀ in dogs is 40 mg/kg, and lethal doses in dogs, cats and most farm animals is 20–40 mg/kg. Limited data show that birds are more susceptible (LD₅₀ in doves is 10–20 mg / kg) than mammals. Theoretically, species that are able to vomit protect themselves by doing so.

Absorption, metabolism, and excretion

Zinc phosphide rapidly breaks down in the acid stomach environment to the toxic phosphine, which readily undergoes absorption. If ingested on an empty stomach, there is less acid present (pH>5) and virtually no phosphine is produced. The metabolism and excretion of phosphine is not well known. Some phosphide is also absorbed.

Mode of action

The toxicity of metal phosphides arises from the rapid liberation of phosphine gas by acid hydrolysis in the stomach (faster with lower pH) or (less rapidly) by contact with moisture. Phosphine is an extremely irritating cytotoxic gas, primarily affecting the

heart, liver, and lungs, but the kidney can also be markedly affected. Phosphine also causes non-specific depression of the hematopoietic system, resulting in anaemia. Phosphides are also directly toxic in the stomach, inducing pain and emesis in dogs and cats, and are partly absorbed, mainly harming the liver and kidney. The predominant cause of death is pulmonary oedema and tissue anoxia.

Non-target effects

Zinc phosphide is a non-specific toxicant. Factors affecting the risk of poisoning are disposition of bait, presence of NTA, weight of animal eating the bait, and the innate ability of the animal to vomit (not possible in rodents and rabbits).

Diagnosis of zinc phosphide poisoning

The diagnosis of zinc phosphide poisoning is difficult, as signs are non-specific. Only analysis of vomit or stomach content can specifically determine poisoning in the animal.

Onset of clinical signs

The occurrence, speed of onset, and severity of signs is dose-dependent. Lethal doses induce signs within 15 minutes to 4 hours after ingestion, rarely up to 18 hours. Animals usually die in 3–5 hours.

Clinical signs

- Zinc phosphide has similar systemic toxicity effects to phosphorus.
- Vomiting, sometimes bloody, is common in dogs and cats.
- Severe depression and weakness are also marked, but pain and CNS effects may sometimes be manifested by vocalisation, wild running and snapping.
- Respiration becomes rapid and noisy.
- Tremor, hyperaesthesia, salivation, extensor rigidity or seizures may be seen.

Laboratory diagnosis

- The freshly opened stomach contents may have a characteristic acetylene or fishy smell.

- Necropsy changes seen are non-specific. There may be congestion and oedema in the lungs, pale yellow liver and fatty kidney.
- Histopathological lesions in acute or subacute cases have included pulmonary congestion and oedema, fatty degeneration and necrosis of liver and kidney, and some cardiac necrosis.
- Vomitus or stomach contents can be analysed for phosphide and for zinc. Excess zinc can also be determined in the blood. There are rapid qualitative tests for phosphide (sensitivity about 50 ppm) that can be performed on stomach contents.

Treatment of zinc phosphide poisoning in animals

There is no antidote to zinc phosphide poisoning, so treatment is mainly supportive and symptomatic after efforts to reduce absorption.

- Emesis is characteristic, but not invariable, in this toxicosis. If ingestion was recent (<1 hour), and emesis has not occurred, it can be induced. Activated charcoal should be given, even though its efficacy has not been proven.
- The stomach pH should be elevated by orally administering 50 ml of a 3–5% sodium bicarbonate solution, or (also in a home setting) 10–50 ml of a hydroxide-based human antacid preparation.
- Mineral oil, which solubilises the toxicant, prevents absorption, and acts as a cathartic, can be given orally at about 1.5 ml/kg. Activated charcoal is probably not effective.
- Gastric lavage using 50-150 ml of a 0.02% potassium permanganate solution may convert the phosphide to harmless phosphate.
- An IV line should be made and fluids given to correct metabolic acidosis, hypocalcaemia and shock. Sodium, potassium, calcium, glucose, acid-base status, and liver and kidney function are further monitored by blood testing.
- Lung oedema (seen in chest radiograph) and respiratory distress should be dealt with by administering oxygen and mechanical ventilation. If lung oedema is suspected, and there is no hypovolaemia, the diuretic furosemide may help.

- If liver damage is recorded, supportive vitamin K₁, B vitamins and a special diet may be given.
- Cardiac function can be monitored by ECG.
- Supportive therapy using calcium borogluconate, bronchodilators, plasma expanders, vasopressors, digoxin and pain control should be considered.

References

Eason, C.T.; Wickstrom, M. 2001: Vertebrate pesticide toxicology manual (Poisons). *Department of Conservation Technical Series 23*, Department of Conservation, Wellington, NZ.

Knight, M.W. 2001: Zinc phosphide. *In*: Peterson, M.E.; Talcott, P.A. eds Small animal toxicology. W.B. Saunders, Philadelphia, USA. Pp. 748–755.

Osweiler, G.D. 1996: Posphides of zinc, aluminum, or calcium. *In*: Toxicology. Williams and Wilkins, Philadelphia, USA. Pp. 282–284.

Section 3: First aid in human intoxications

General first-aid notes

Despite what many people may think, no substance is inherently safe or unsafe. Any substance – even the most innocuous – can be harmful if you are exposed to too much of it. The potential for a pesticide to cause injury depends upon several factors:

- **Toxicity.** Toxicity is the potential a chemical, such as a pesticide, has for causing harm. Some pesticides have low human toxicity while others are extremely toxic.
- **Dose.** The greater the quantity of a chemical you are exposed to, the greater the risk of injury. The effect of a given dose varies with the weight and age of the person. Therefore, an amount that is relatively harmless to an adult may hurt a small child.
- **Route of absorption.** (The ways the body comes in contact with chemicals). Some common routes of exposure are dermal (skin), oral (by mouth), and inhalation (breathing). Swallowing a pesticide usually creates the most serious problem. In practice, however, the most common route of absorption of pesticides is through the skin.
- **Duration of exposure.** The longer a person is exposed, the more chemical their body absorbs.
- **Physical and chemical properties.** Some pesticides evaporate more readily than others, so they can be more easily inhaled. Some break down quickly on surfaces, others last longer. These qualities affect the potential risk of overexposure.
- **Population at risk.** Persons who run the greatest danger of pesticide illness are those whose exposure is highest, such as workers who mix or apply pesticides.

Recognising pesticide poisoning

Like other chemicals, pesticides may produce injury externally or internally.

Pesticides can cause contact-associated skin irritation or allergies. Symptoms of irritation include redness, itching, or pimples. Allergic skin reactions may produce

redness, swelling, or blistering. The mucous membranes of the eyes, nose, mouth, and throat are also quite sensitive to chemicals. Stinging and swelling can occur.

Internal injuries may occur depending upon where a chemical is transported in the body or what organ is affected. Shortness of breath, excessive saliva and rapid breathing may occur because of lung injury. Other symptoms to watch for include nausea, vomiting, diarrhoea, headache, or dizziness.

General principles for treating acute pesticide poisonings

Specific recommendations for managing acute pesticide poisoning vary among the different types of pesticide. For specific information on treatment, seek medical advice or call the National Poisons Centre 0800 764 766.

Induction of vomiting as a first-aid measure

Evidence and common sense indicate that inducing vomiting is not necessary in most situations where there has been a chemical ingestion. Some of the arguments against inducing vomiting are:

The amount of chemical accidentally ingested by an adult is generally estimated to be very small (about 14–21 mL) (Gosselin et al. 1984).

There is no conclusive evidence that victims of chemical ingestion who do have their stomachs emptied have more successful outcomes than victims who do not (Rumack et al. 1981, Kulig et al. 1985).

There may be significant risks associated with inducing vomiting, especially in emergency situations. For example, vomiting may result in the inhalation of stomach contents (aspiration). The risk of aspiration depends on the physical properties of the chemical and/or the level of consciousness of the victim. Vomiting a corrosive could significantly increase damage to the mouth, throat and oesophagus when the chemical contacts these sensitive tissues for a second time. In an emergency it is not always possible to determine the nature of the chemical that has been ingested. The harm incurred by erroneously inducing vomiting for any of these chemicals would seem to outweigh any possible benefits.

There does not seem to be a reliable and safe first-aid procedure for inducing vomiting in adults. For example, stimulation of the back of the throat with the finger, a spoon or some other blunt object often fails to induce vomiting. When it is successful, it rarely results in productive vomiting. In addition, this procedure may mechanically damage the back of the throat. Syrup of ipecac may not be as effective in adults as in children and may take 15–30 minutes to work. During this time the victim's condition could deteriorate, increasing the risk of aspiration. Copper sulphate and salt water are poor inducers of vomiting and it is possible to give excessive, possibly toxic, doses of these materials. Rapid ingestion of a large volume of water is unreliable. If it does not induce vomiting, dilution of the ingested chemical with a large volume of water can enhance absorption through the stomach (Chin 1971; Easom et al. 1979; Gossel et al. 1981).

Medical attention is usually available quite quickly in most situations. Medical professionals can then determine if the stomach should be emptied and perform the procedure, if necessary.

In 1997 the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists issued a joint position statement on the use of ipecac as an agent for inducing vomiting.

Syrup of ipecac should not be administered routinely in the management of poisoned patients. In experimental studies the amount of marker removed by ipecac was highly variable and diminished with time. There is no evidence from clinical studies that ipecac improves the outcome of poisoned patients and its routine administration in the emergency department should be abandoned. There are insufficient data to support or exclude ipecac administration soon after poison ingestion. Ipecac may delay the administration or reduce the effectiveness of activated charcoal, oral antidotes, and whole bowel irrigation. Ipecac should not be administered to a patient who has a decreased level or impending loss of consciousness or who has ingested a corrosive substance or hydrocarbon with high aspiration potential.

In light of these arguments, induction of vomiting should rarely be recommended for chemical exposures and should only be performed by first-aiders when the chemical is very acutely toxic and medical follow-up is not readily available. In these cases, first aiders should receive special training on how to induce vomiting safely and effectively in the appropriate circumstances.

References

Chin, L. 1971: Gastrointestinal dilution of poisons with water: an irrational and potentially harmful procedure. *American Journal of Hospital Pharmacy* 28: 712–714.

Easom, J.M. et al. 1979: Efficacy and safety of gastrointestinal decontamination in the treatment of oral poisoning. *Pediatric Clinics of North America* 26: 827–836.

Gossel, T.A. et al. 1981: The right first aid for poisoning. *RN* 44(3): 73–75.

Gosselin, R.E. et al. 1984: Clinical toxicology of commercial products, 5th edition. Williams & Wilkins, Baltimore. Pp. 11–118.

Kulig, K. et al. 1985: Management of acutely poisoned patients without gastric emptying. *Annals of Emergency Medicine* 14: 562–567.

Rumack, B.H. et al. 1981: Emesis: safe and effective? *Annals of Emergency Medicine* 10: 551.

Section 4: Signs and symptoms of poisoning and first aid for specific vertebrate pesticides

1080

Signs and symptoms

- There is a delay in onset of symptoms of at least 30 minutes to 2.5 hours. In one case there was a 20-hour delay before major symptoms (Reigart et al. 1975).
- Nausea, apprehension and agitation are most commonly observed. In one review of 38 intentional ingestions, the most frequent symptom was nausea or vomiting (either or both in 74% of cases) (Chi et al. 1996). Other symptoms included diarrhoea and abdominal pain.
- More seriously, depressed consciousness leading to coma, convulsions and respiratory distress followed by depression can occur.
- Hypotension, atrial fibrillation, ventricular premature beats or tachycardia may also be noted.
- Hypocalcemia and hypokalemia along with significant metabolic acidosis were also found often in this case series (Chi et al. 1996). The most frequent ECG findings were non-specific ST segment and T wave abnormalities (in about 72% of cases). The authors concluded that marked hypotension (systolic blood pressure <90 mmHg) and the early onset of metabolic acidosis and increased serum creatinine are associated with poor short-term survival (Chi et al. 1996).

Toxicity to humans

Reported human fatal doses have ranged from 0.714 mg/kg to 5 mg/kg (RTECS 1996). The typical human fatal dose quoted is 2 mg/kg (Ellenhorn & Barceloux 1988), but it appears from the above data that less than 1 mg/kg could occasionally be fatal or at least

seriously toxic. One review suggests that doses of 0.5–2.0 mg/kg should be considered highly dangerous (Hayes & Laws 1991).

Cereal or carrot baits (containing 1.5 mg 1080/g bait, i.e. 0.15% concentration) are used for both aerial and bait-station control of possums in New Zealand. The 1080 is dissolved in water before being added to baits. The estimated typical fatal dose for a 75kg adult from these cereal or carrot baits is about 100 g.

Currently poisoning is uncommon in children. Six pellets of possum bait could seriously endanger the life of a small child, though a single pellet would be unlikely to cause any symptoms. Most case reports concern use of 1080 overseas as a home-based rodenticide (Gaidusek & Luther 1950; Brockman 1955; Reigart et al. 1975) although contaminated wheat has been the source on one occasion (McTaggart 1970).

First-aid treatment for 1080 poisoning

Speed is essential. Obtain immediate ambulance and medical attention. Call 111.

- **Inhalation.** If ill effects occur, remove person to fresh air. Keep patient warm and quiet and seek medical advice.
- **Skin contact.** Flush well with plenty of soap and water while removing contaminated clothing. If a large area is affected, seek medical advice.
- **Eye contact.** Immediately irrigate with water for at least 10–15 minutes seek medical advice.
- **Ingestion.** Do not administer water or milk. Large amounts of alcoholic spirits (e.g. whisky, gin, brandy) and large amounts of cane sugar (ordinary sugar) may prove useful, although unproven. Seek medical attention immediately.

References

Brockman, J.L. et al. 1955: Fatal poisoning with sodium fluoroacetate. *JAMA* 159: 1529–1532.

Ellenhorn, M.J.; Barceloux, D.G. 1988: Medical toxicology. Elsevier, New York.

Chi, C-H. et al. 1996: Clinical presentation and prognostic factors in sodium monofluoroacetate intoxication. *Clinical Toxicology* 34: 707–712.

Gaidusek, D.; Luther, G. 1950: Fluoroacetate poisoning. *American Journal of Diseases of Children* 104: 310–321.

Hayes, W.J.; Laws, E.R. eds 1991: Handbook of pesticide toxicology. Academic Press, London.

McTaggart, D.R. 1970: Poisoning due to sodium fluoroacetate (1080). *Medical Journal of Australia (Oct)*: 641–642.

Reigart, J.R. et al. 1975: Sodium fluoroacetate poisoning. *American Journal of Diseases of Children* 129: 1224–1226.

RTECS (Registry of Toxic Effects of Chemical Substances) 1996: Cincinnati (OH): National Institute for Occupational Safety and Health. Cheminfo CD Rom. Version 96-4. Canadian Centre for Occupational Health and Safety, Hamilton, Ontario.

Cyanide

Signs and symptoms

In cases where cyanide intoxication is not rapidly overwhelming, the patient may experience flushing, involuntary gasping/tachypnoea, tachycardia, headache and dizziness. Progressive poisoning leads to agitation, diminishing level of consciousness, bradycardia, hypotension, seizures and coma. Death generally follows cardio-respiratory failure. Pulmonary oedema is well recognised in those suffering severe exposures.

While classically described as presenting with cherry red skin colouring, patients with significant cyanide intoxication often present cyanosed (van Heijst et al. 1987). Hallmark indicators of cyanide poisoning include loss of consciousness, metabolic acidosis (with increased anion gap), followed by cardiopulmonary distress (Yen et al., 1995). While the smell of bitter almonds may be used as a diagnostic clue, it cannot be relied upon as many individuals cannot detect the odour.

Severity of poisoning (Meredith et al. 1993)

Mild toxicity. Nausea, dizziness, drowsiness.

Moderate toxicity. Loss of consciousness for a short period, convulsion, vomiting, cyanosis.

Severe toxicity. Deep coma, dilated non-reactive pupils, deteriorating cardio-respiratory function.

Acute effects (route of exposure)

Inhalation

An initial response following exposure to hydrogen cyanide gas is deep gasping breaths, further increasing intoxication. Inhalation of cyanide gas is generally lethal within

minutes and medical aid often too late to be lifesaving. Those individuals able to effect self-rescue from the source of gas are highly unlikely to suffer further ill effects if conscious 5 minutes after exposure has ceased.

Ingestion

Cyanide compounds may produce a bitter, pungent, burning taste in the mouth, and oral and gastric corrosion. While death may be rapid following ingestion, this is dependent upon such factors as dose, gastric pH, presence of food in the stomach, and type of cyanide salt. Indeed while symptoms may occur within minutes, death may be delayed by hours (van Heijst et al. 1987). The majority of patients will make a full recovery if surviving the acute intoxication; a proportion may suffer anoxic organ damage.

Skin

Both liquid and gaseous forms of cyanide can be absorbed across the skin producing systemic poisoning (Walton & Witherspoon 1925; Lam & Lau 2000).

Eye

Cyanide liquids are irritating and absorbed by the mucus membrane. Hydrogen cyanide gas is also absorbed and may damage the retina and optic nerve.

Injection

Parenteral exposure allows near instantaneous absorption and by-pass of first-pass metabolism. A lethal dose of cyanide will produce death more rapidly than by ingestion.

First-aid treatment for cyanide poisoning

Speed is essential. Obtain immediate ambulance and medical attention. Call 111. Protect yourself and the casualty from further exposure during decontamination and treatment.

- **Inhalation.** Remove patient from exposure. Keep warm and at rest. If the person is sleepy or unconscious: Check their pulse, ensure they are breathing, and place them in the recovery position: Lay the person on their side and ensure their head is lower than their body. Oxygen should be administered. If breathing has ceased apply

artificial respiration using oxygen and a suitable mechanical device such as a bag and mask. Do not use mouth-to-mouth resuscitation as you may poison yourself.

- **Skin contact.** Remove all contaminated clothing immediately using gloves. Wash the skin with plenty of water and soap. Treat patient as for inhalation.
- **Eye contact.** Immediately irrigate with water for at least 10–15 minutes. Treat patient as for inhalation.
- **Ingestion.** Do not give anything by mouth. Do not make them vomit. Treat patient as for inhalation.

Poisoning management discussion

Decisions about treatment will vary depending on the circumstances; however, general treatment for mild exposure to cyanide includes oxygen and bed rest. Treatment for moderate to severe exposure includes oxygen and antidotes. Where cyanide has been ingested the patient should not be induced to vomit as the expelled stomach contents may be contaminated or hydrogen cyanide gas may also be expelled.

Following ingestion of cyanide salts, patients may present a hazard to healthcare providers due to production of hydrogen cyanide gas from reaction of the cyanide salt with stomach acid. This may be exhaled by the patient, or can evolve from vomit.

Amyl nitrite, given by inhalation, has been used since the 1930's as a cyanide antidote (Cheen et al. 1934), although there is little scientific evidence that it is of significant benefit. While the initial mode of action was thought to be due to generation of the cyanide binding methaemoglobin, it has subsequently been concluded that there may be another, possibly vasoactive, mechanism at work (Way et al. 1984; Vick & Froelich 1985). It is also potentially dangerous, particularly in people with some forms of heart disease, although serious illness caused by misuse seems to be rare. It can be abused by “sniffers”. It also has a limited shelf life and can be difficult to obtain as it is manufactured only in small quantities. Its use is still described in safety data sheets and there may be circumstances, such as the use of cyanide preparations in the field for control of rodents, where it is the only treatment that can practicably be given. However, to be effective this antidote must be used at high inhalational doses, and in conjunction with high concentrations of oxygen.

References

Cheen, K.K.; Rose, C.L.; Clowes, G.H.A. 1934: Comparative values of several antidotes in cyanide poisoning. *American Journal of the Medical Sciences* 188: 767–781.

Lam, K.K.; Lau, F.L. 2000: An incident of hydrogen cyanide poisoning. *American Journal of Emergency Medicine* 18: 172–175.

Meredith, T.J.; Jacobsen, D.; Haines, J.A.; Berger, J-C.; van Heijst, A.N.P. eds 1993: IPCS/CEC evaluation of antidotes series, 2: Antidotes for poisoning by cyanide. Cambridge University Press, Cambridge. P. 15.

van Heijst, A.N.P.; Douze, J.M.C.; van Kesteren, R.G. 1987: Therapeutic problems in cyanide poisoning. *Journal of Toxicology – Clinical Toxicology* 25: 383–398.

Vick, J.A.; Froelich, H.L. 1985 Studies on cyanide poisoning. *Archives Internationales de Pharmacodynamie et de Therapie* 273: 314–322.

Walton, D.C.; Witherspoon, M.G. 1925: Skin absorption of certain gases. *Journal of Pharmacology and Experimental Therapeutics* 26: 315–324.

Way, J.L.; Sylvester, D.; Morgan, R.L. et al. 1984: Recent perspectives on the toxicodynamic basis of cyanide antagonism. *Fundamental and Applied Toxicology* 4: S231–239.

Yen, D.; Tsai, J.; Wang, L-M. et al. 1995: The clinical experience of acute cyanide poisoning. *American Journal of Emergency Medicine* 13: 524–528.

Anticoagulant rodenticides

Signs and symptoms

Haemorrhage is the hallmark of anticoagulant poisoning (Landefeld & Beyth 1993). Time of onset is dependent on depletion of vitamin-K-dependent coagulation factors (II, VII, IX, X). While decreased coagulation may be noted as early as 8–12 hours after ingestion, peak effects are not seen for 1–3 days. Intra-cranial haemorrhage and shock resulting from blood loss are recognised causes of death.

Acute effects (route of exposure)

Inhalation

Animal studies confirm that oral anticoagulants can cause toxicity following absorption via the respiratory tract (Tomlin 1997). A case of coagulopathy has been reported after chronic smoking of marijuana mixed with brodifacoum (a "second generation" coumarin anticoagulant or "superwarfarin") (La Rosa et al. 1997).

Skin

Animal studies confirm oral anticoagulants can be absorbed significantly through the skin and cause toxicity; anticoagulant rodenticides are also recognised to cause slight to mild skin irritant (Tomlin 1997). Warfarin-contaminated talcum powder was responsible for the death of 117 children following dermal application; (Martin-Bouyer 1983) and intra-cranial haemorrhage has occurred following unprotected handling of warfarin-containing rat bait (Abell et al. 1994).

Toxicity

The coumarin anticoagulant compounds are toxic via ingestion, inhalation, and dermal exposure, and are noteworthy in being more hazardous when the same total amount is taken in divided doses over several days than as a single one-off dose. Persons already on anticoagulant therapy are at increased risk from a given amount.

A dose of 1 mg brodifacoum (approximately 0.014 mg/kg, equivalent to 20 g of 0.005% bait) in an adult caused symptoms of anticoagulation, which persisted for 76 days (Chen & Deng 1986).

A higher dose, about 0.12 mg/kg, produced a prolonged (7-week) coagulation disturbance in an adult (Jones et al. 1984).

The largest recorded ingestion was 75 mg brodifacoum (approximately 1.1 mg/kg) ingested over a 2-day period in a 31-year-old female. The patient survived with treatment, but prothrombin levels did not normalise for 8 months (Lipton & Klass 1984).

There are no accurately estimated amounts of ingested brodifacoum in any reported cases of toxic effects in children. A retrospective review of 10 762 single, acute, unintentional ingestions of brodifacoum by children aged six or less found no instances of major effects or death (Shepherd et al. 2002).

First-aid treatment for anticoagulant poisoning

- **Inhalation.** If ill effects occur, remove person to fresh air. Keep warm and quiet and seek medical advice.
- **Skin contact.** Flush well with plenty of soap and water while removing contaminated clothing. Seek medical advice.
- **Eye contact.** Immediately irrigate with water for at least 10 minutes and seek medical advice.
- **Ingestion.** Do not induce vomiting. Do not give fluids to dilute. Seek medical attention.

References

Abell, T.L.; Merigian, K.S.; Lee, J.M. et al. 1994: Cutaneous exposure to warfarin-like anticoagulant causing an intracerebral hemorrhage: a case report. *Journal of Toxicology – Clinical Toxicology* 32: 69–73.

- Chen, T.W.; Deng, J.F. 1986: A brodifacoum intoxication case of mouthful amount (Abstract). *Veterinary and Human Toxicology* 28: 488.
- Jones, E.C.; Growe, G.H.; Naiman, S.C. 1984: Prolonged anticoagulation in rat poisoning. *JAMA* 252: 3005-3007.
- Landefeld, C.S.; Beyth, R.J. 1993: Anticoagulant-related bleeding: clinical epidemiology, prediction, and prevention. *American Journal of Medicine* 95: 315–328.
- La Rosa, F.G.; Clarke, S.H.; Lefkowitz, J.B. 1997: Brodifacoum intoxication with marijuana smoking. *Archives of Pathology and Laboratory Medicine* 121: 67–69.
- Lipton, R.A.; Klass, E.M. 1984: Human ingestion of a 'superwarfarin' rodenticide resulting in a prolonged anticoagulant effect. *JAMA* 252: 3004–3005.
- Martin-Bouyer, G.; Khanh, N.B.; Linh, P.D. et al. 1983: Epidemic of haemorrhagic disease in Vietnamese infants caused by warfarin-contaminated talcs. *Lancet* 1: 230–232.
- Shepherd, G.; Klein-Schwartz, W.; Anderson, B.D. 2002: Acute, unintentional pediatric brodifacoum ingestions. *Pediatric Emergency Care* 18: 174–178.
- Tomlin, C.D.S. ed. 1997: The pesticide manual, 11th edition. British Crop Protection Council, Farnham.

Cholecalciferol

Signs and symptoms

The symptoms seen are due to the consequences of acute and chronic hypercalcaemia.

The earliest symptoms include gastrointestinal effects, generalised weakness, drowsiness, headache, fatigue, myalgia, ataxia, tinnitus and hypotonia (McEvoy 1995).

Major concerns are the risk of acute-hypercalcaemia-induced arrhythmias and long term tissue deposition of calcium (calcinosis) at critical sites.

In animals, at least, there may be a 2–3 day delay before onset of clinical signs (Talcott & Mather 1991).

Toxicity

Adult. Limited data are available for toxicity due to single overdose; however, one source suggests that 4 000 000 IU is necessary to produce acute hypercalcaemia (Brin 1976).

First aid treatment for cholecalciferol poisoning

- **Inhalation.** If ill effects occur, remove person to fresh air. Keep warm and quiet and seek medical advice.
- **Skin contact.** Flush well with plenty of soap and water while removing contaminated clothing. Seek medical advice.
- **Eye contact.** Immediately irrigate with water for at least 10 minutes and seek medical advice.
- **Ingestion.** Do not induce vomiting. Do not give fluids to dilute. Seek medical attention.

References

Brin, M. 1976: Toxicology of vitamin D. Report of Second Wyeth Nutrition Symposium, 1976.

McEvoy, G.K. *ed.* 1995: AHFS Drug Information. Bethesda (MD): American Society of Health-System Pharmacists. Pp. 2535–2538.

Talcott, P.A.; Mather, G.G. 1991: Accidental ingestion of a cholecalciferol-containing rodent bait in a dog. *Veterinary and Human Toxicology* 33: 252–256.

Phosphorus

Signs and symptoms

Phosphorus causes tissue destruction, with disturbance of the carbohydrate, fat and protein metabolism in the liver.

Pathological findings in acute yellow phosphorus poisoning are jaundice, fatty degeneration and necrosis of the liver and kidneys, haemorrhage, congestion, and erosion of the gastrointestinal tract. Pathological findings from phosphine inhalation are pulmonary hyperaemia and oedema. Zinc or aluminium phosphide ingestion cause both fatty degeneration and necrosis of the liver and pulmonary hyperaemia and oedema.

Acute effects (route of exposure)

Ingestion

Ingestion leads to local gastrointestinal effects and, if enough phosphorus is absorbed, signs of systemic poisoning. Systemic absorption can lead to cardiovascular collapse, hepatic or renal failure and death.

Nausea, vomiting, diarrhoea, and abdominal pain generally develop within minutes to hours of ingestion. The patient's faeces or vomitus may have a garlic odour and have occasionally been observed to smoke. In serious cases tachycardia, hypotension and shock may occur. Liver and renal injury may follow (Diaz-Rivera et al. 1950).

Death in coma may occur within 24–48 hours, or symptoms may improve for 1–2 days and return, with nausea, vomiting, diarrhoea, liver tenderness and enlargement, icterus, prostration, fall of blood pressure, oliguria, hypercalcaemic tetany, and multiple petechial haemorrhages. Coma with Cheyne Stokes respiration, convulsions and death may occur up to 3 weeks after poisoning.

Skin

Yellow phosphorus allowed to dry on the skin will ignite and cause second- or third-degree burns surrounded by blisters. These burns heal slowly (Monzingo et al. 1988)

Chronic effects

Inhalation

Chronic, low-level exposure to white phosphorus or its fumes has been associated with oral and mandibular necrosis, a well-described occupational illness described as phossy jaw (Hughes et al. 1962).

The first symptom is toothache, followed by swelling of the jaw and then necrosis of the mandible. Other findings are weakness, weight loss, loss of appetite, anaemia, and spontaneous fractures.

Toxicity

Persons ingesting more than 1 mg/kg of yellow phosphorus are at risk of severe toxicity and death is likely to occur following the ingestion of 1 g (Diaz-Rivera et al. 1950).

First-aid treatment for phosphorus poisoning

Speed is essential. Obtain immediate ambulance and medical attention. Call 111. Protect yourself and the casualty from further exposure during decontamination and treatment.

- **Inhalation.** If ill effects occur, remove person to fresh air. Keep warm and quiet and seek medical advice.
- **Skin contact.** Remove all contaminated clothing immediately using gloves. Wash the skin with plenty of water and soap and seek medical attention.
- **Eye contact.** Immediately irrigate with water for at least 10 minutes and seek medical advice.
- **Ingestion.** Do not give anything by mouth. Do not induce vomiting. Seek urgent medical attention.

References

Diaz-Rivera, R.S.; Collazo, P.J.; Pons, E.R. et al. 1950: Acute phosphorus poisoning in man: a study of 56 cases. *Medicine* 29: 269–298.

Hughes, J.P.; Baron, R.; Buckland, D.H. et al. 1962: Phosphorus necrosis of the jaw: a present day study. *British Journal of Industrial Medicine* 19: 83–99.

Monzingo, D.W.; Smith, A.A.; McManus, W.F. et al. 1988: Chemical burns. *Journal of Trauma* 28: 642–647.

Zinc phosphide

Signs and symptoms (acute)

These include nausea, vomiting, hypotension, dyspnoea, and altered mental status. Immediate death results from pulmonary oedema. Hepatic, cardiac and renal injury may occur. Death may occur up to a week after poisoning and is often due to cardiotoxicity (Stephenson 1967).

Toxicity

Ingestion of as little as 4 g of zinc phosphide has been lethal, but survival has occurred after ingestions of up to 50 g (Stephenson 1967). The toxicity of zinc phosphide is fully accounted for by the toxicity of the phosphine it produces when hydrolysed by the acid of the stomach (von Oettingen 1947).

Workers engaged in the fumigation of grain stores with phosgene have reported coughing, dyspnoea, chest tightness, headache, dizziness, numbness, lethargy, anorexia, diarrhoea, nausea, epigastric pain, and vomiting (Jones et al. 1964)

The dangerous concentration in air of phosphine is 0.05 ppm.

First-aid treatment for zinc phosphide poisoning

Speed is essential. Obtain immediate ambulance and medical attention. Call 111. Protect yourself and the casualty from further exposure during decontamination and treatment.

- **Inhalation.** Remove patient from exposure. Keep warm and at rest. If the person is sleepy or unconscious: Check their pulse, ensure they are breathing, and place them in the recovery position: Lay the person on their side and ensure their head is lower than their body. Do not use mouth-to-mouth resuscitation as you may poison yourself.
- **Skin contact.** Remove all contaminated clothing immediately using gloves. Wash the skin with plenty of water and soap and seek medical attention.

- **Eye contact.** Immediately irrigate with water for at least 10 minutes and seek medical advice.
- **Ingestion.** Do not give anything by mouth. Do not induce vomiting. Seek immediate medical attention.

References

Jones, A.T.; Jones, R.C.; Longley, E.O. 1964: Environmental and clinical aspects of bulk wheat fumigation with aluminium phosphide. *American Industrial Hygiene Association Journal* 25: 376–379.

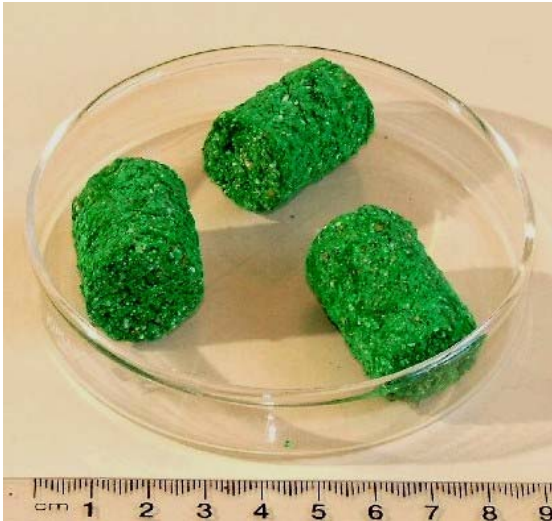
Stephenson, J.B.P. 1967: Zinc phosphide poisoning. *Archives of Environmental Health* 15: 83–88.

Von Oettingen, E.W. 1947: The toxicity and potential dangers of zinc phosphide and hydrogen phosphide (phosphine). *Public Health Report* 203: 1–17.

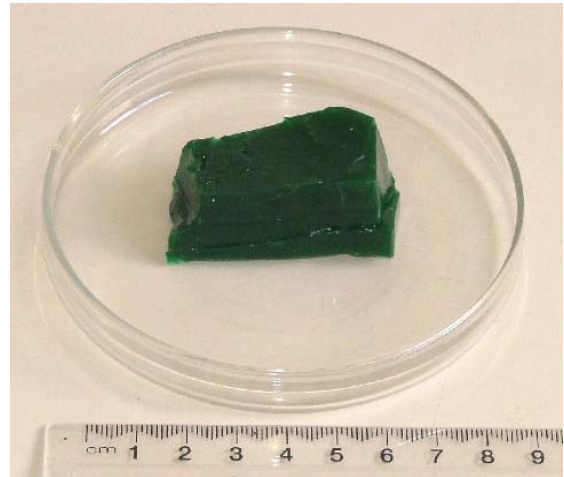
Section 5: Pictures of baits

1080 Baits

Animal Control Products 1080 cereal
bait

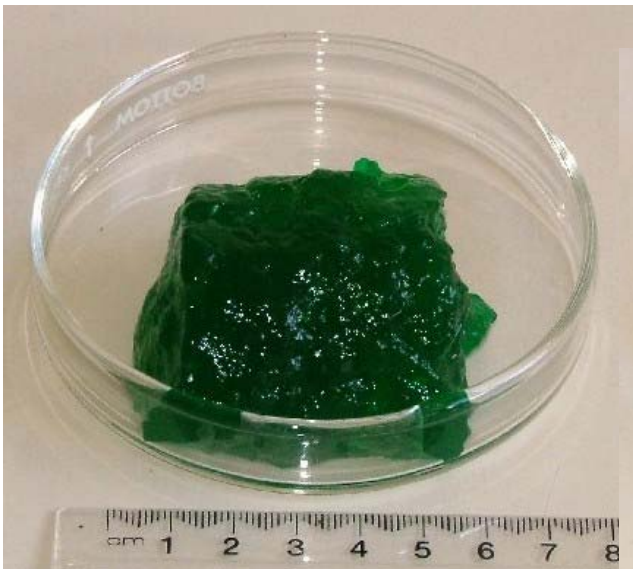


Kiwicare 1080 gel bait

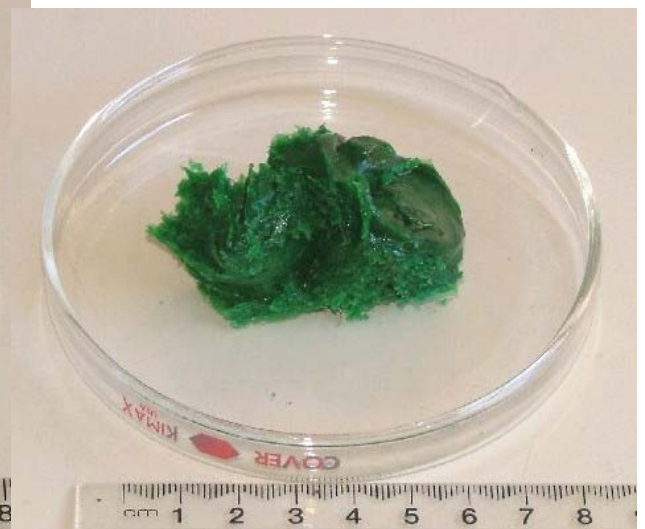


Cyanide Baits

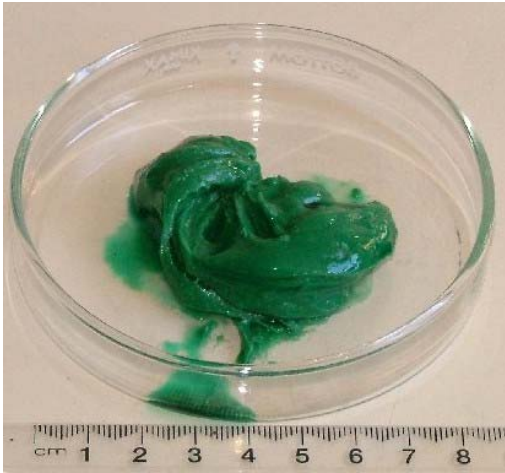
Animal Control Products 1080 Gel bait



Animal Control Products Cyanide Paste
for Possum Destruction



Animal Control Products Pestoff
Exterminator Paste

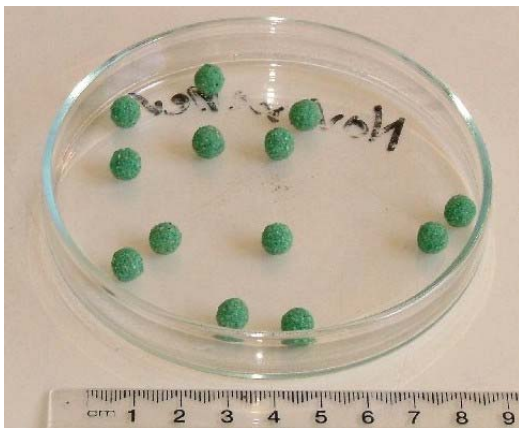


Brodifacoum baits

Animal Control Products Pestoff
Possum bait



Feratox



Animal Control Products Pestoff Waxed
Possum bait



Ferapaste

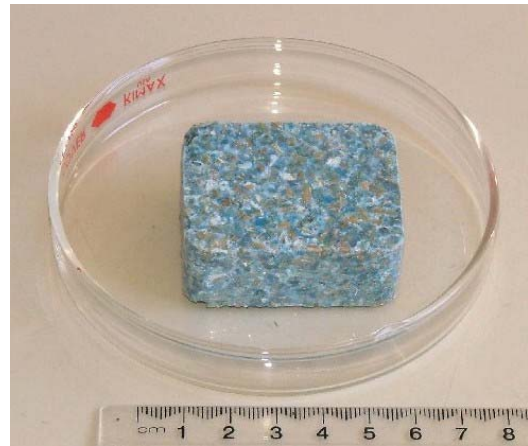


Bromadiolone

Confrac



Kiwicare No Rats and Mice
Weatherproof Bait Blocks



Coumatetralyl

Kiwicare No Rats and Mice Bait and
Tracking Powder



Diphacinone

Animal Control Products Pestoff Ferret
Paste

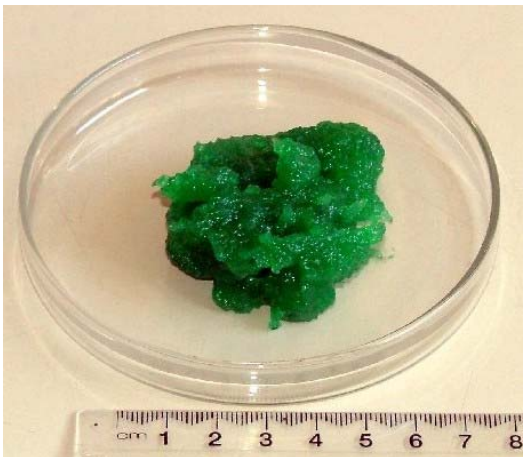


Ditrac



Phosphorus

Animal Control Products Phosphorised
Paste



Section 6: Recommended basic kit for veterinarians

Activated charcoal	Sodium nitrite
Sorbitol	Vitamin K ₁
Gastric lavage set	Frozen plasma
Apomorphine	Saline
Xylazine	Furosemide
Oxygen	Prednisone
Ringer solution	Calcitonin
Lactated ringer solution	Metoclopramide
Isotonic crystalloids	Sodium EDTA
Hetastarch/Hemacel/Dextran 70	Pamidronate disodium
B vitamins	Mineral oil
Diazepam	Potassium permanganate
Pentobarbitone	Copper sulphate
Methocarbamol or glycerol guaicolate	Hydrogen peroxide
Calcium gluconate	Sodium bicarbonate
Lidocaine or procainamide	Sucralfate
Sodium thiosulphate	