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3RD EDITION

Veterinary Clinical Toxicology

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VETERINARY CLINICAL TOXICOLOGY

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Preface

The early settlers of New Zealand had to learn the hard way and the livestock losses from the ingestion of poisonous plants and other materials reported in the colonial era are fascinating to read.

It is to the credit of subsequent generations of veterinarians and research workers that very significant contributions have been made to our knowledge of many of the sophisticated diseases of grazing animals, notably the mycotoxicoses.

In addition there are now many recorded case histories, particularly in the New Zealand Veterinary Journal, Vetscript New Zealand and the Surveillance reports of the Ministry of Agriculture and Forestry. These are rich in detailed information on the occurrence, diagnosis and treatment of animal poisoning.

This edition is a complete revision of the previous publication which is the basis of the course in Veterinary Clinical Toxicology, taught to New Zealand veterinary students. A number of new additions have been added and every attempt made to present both students and practicing veterinarians with a composite and ready reference on the subject.

Over 925 references are given in this edition. Many of these refer to New Zealand experiences. In particular, the numerous references from the Quarterly Diagnostic Reports of Surveillance will prove valuable for practitioners experiencing a toxicological problem for the first time. Readers are encouraged to study these as they contain a wealth of helpful circumstantial information. They can be easily accessed on www.sciquest.org.nz

In some sections, the information has been summarized from published sources and if there is the occasional identical wording to these no apology is made, since no better phrases could be imagined.

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Clinical Toxicology

The Diagnosis of Poisoning

The diagnosis of poisoning requires a wide range of clinical skills. When toxicosis occurs, there is often no clear evidence of exposure to a poison. Frequently the animals are just found dead, moribund or showing generalised clinical effects that could well be produced by a variety of clinical agents.

There are literally hundreds of poisons of chemical and plant origin to which animals are at risk and in any given text it is only possible to deal with those which commonly occur and those which may be peculiar to a country or a region.

It must also be remembered that the effect of poisons may be quite different between the species. The veterinary surgeon dealing now-a-days with several grazing species of animals as well as monogastric species, has a very difficult task to be conversant with the extensive range of poisons affecting these animals. Therefore it is important that a clinical procedure is followed in all toxicological investigations, for not infrequently the veterinary surgeon is called to investigate a problem not experienced previously.

Further as the range of herbicides, dips, drenches, and pesticides extends and changes, new toxicological situations arise which call for new knowledge in both diagnosis and therapy. Some previously common toxicological problems in New Zealand are now uncommon. For example, previously there were many cases of strychnine, cyanide, arsenic, organochlorine and paraquat poisoning. Some of these have been removed from sale (e.g. arsenical dips), while others such as cyanide has varied in popularity as a possum poison. On the other hand because of the continued use of 1080 in possum baits, accidental poisoning from it is still prevalent.

While the basic clinical procedure in toxicological examinations is similar to other medical examinations, much more emphasis is placed on the ability of the clinician to fossic out from the environment just what was the poison to which the animal had access.

Yet another complicating factor in most toxicoses is the urgency required in making a diagnosis and instigating some form of therapy. In brief you are dealing with an emergency and frequently, further animals are at risk if effective action is not taken by the veterinary surgeon and the owner.

As either a veterinary student or a new and inexperienced veterinary surgeon it is vital to follow a regular pattern of investigation so that with experience one becomes thoroughly competent with the special clinical procedure required for toxicological problems. If this is done the veterinarian will find that toxicology is a most rewarding and exciting branch of veterinary science.

Clinical Procedure to establish a diagnosis

The diagnosis of poisoning rests on five components, some of which may be more important than others. A diagnosis may be made from the proper use of only one or two of these components, but it is important to realise that each is an additional back up to your final

diagnosis. Remember also that not infrequently, veterinarians become involved in litigation, so that the more evidence recorded the sounder is your diagnosis and course of action.

The five components required for diagnosis are:

1. Consideration of circumstantial evidence.
2. Clinical signs shown not only in the individual but also other members of the herd or flock as a whole must be considered.
3. Post mortem examination of dead animals and a careful pathological investigation.
4. Clinical pathology tests and chemical analysis of tissues from either dead or living animals, for traces of suspected poisons.
5. Experimental evidence.

1. Circumstantial Evidence

This can be a very broad area of investigation and means the animal's environment must be meticulously examined, both by investigation and careful questioning of the client. Toxicology hazards of the environment may be either naturally occurring or man-made.

a. Naturally-occurring hazards

i. Poisonous minerals - Most problems associated with minerals are local in nature: For example the selenaceous soils of North America, and some regions of both Australia and New Zealand where high copper levels of soil and pasture are seen. Similarly fluorine contaminated waters are a well-recognised hazard in different parts of the world.

ii. Poisonous plants - These represent a highly specialised toxicological hazard. The veterinarian has a responsibility to be conversant with and able to recognise local plants and pastures which may be toxic to grazing animals. Again many of these problems are local in nature and are either associated with the plant directly or fungi which infest them at particular times of the year e.g. facial eczema and ryegrass staggers.

b. Man-made hazards

i. Industrial contamination - Where agriculture and industry are closely associated, contamination of water and herbage by industrial effluents is always likely. Contamination can take place either through atmospheric transfer or where bulk waste is dumped on unused land. In the latter situation flooding may cause leaching and transfer of the waste to surrounding areas. Many examples of industrial contamination and the poisoning of both human and animals can be given.

Materials frequently associated with industrial contamination include, lead, arsenic, fluorine, chromium, phenols, cyanide, alcohol and waste oil.

ii. Herbicides and pesticides - The products included under this heading are numerous. For example the widespread use of the organophosphates for controlling pests of both plants and animals has produced a range of toxicological problems with domestic animals. Further as these products are changed and improved still further toxicoses may arise. A knowledge of all herbicides and pesticides is not possible for the individual so that reference centres must be used.

In spite of warnings on these products there are still many cases of poisoning recorded in New Zealand each year from weed killers, rodenticides, orchard sprays, dips and molluscicides.

iii. Domestic Materials - Domestic materials still account for many cases of individual poisoning, particularly among pet animals. High on the list of frequency is still lead poisoning occurring from paint flakes in particular. Other domestic materials that present a serious risk include sump oil, diesel oil, detergents, antifreeze (ethylene glycol) and salted foods.

iv. Drugs - Poisoning of animals with drugs may occur from using human medication for animals e.g. cats given aspirin or from veterinary therapy using an inappropriate dose schedule.

The incorrect use of drugs by a veterinarian is referred to as iatrogenesis. In the use of drugs, a whole range of individual matters must be considered, including species differences, the vulnerability of the very young and old, and a wider range of factors associated with the animal's ability to biotransform and excrete the particular chemical.

v. Food and Water - There are many examples of poisoning from food and water. Food may be badly harvested and stored as in dicoumarol poisoning with spoiled sweet clover, solanine poisoning from green potatoes, mouldy hay toxicoses, or nitrate poisoning from steeped mangolds. Severe contamination of stored food can also occur. A good example recorded in New Zealand was hyperkeratosis of cattle associated with the feeding of hay which had been stored in a hayshed where chlorinated naphthalenes had been used as a wood preservative. Then there was the serious loss of human lives and livestock and poultry in North America following cattle food contamination with PBB (polybrominated biphenyl, a fire retardant).

2. Clinical Examination

While many symptoms are suggestive of poisoning, few are pathognomonic. Many can be duplicated by several poisons. The range of clinical signs for any poisoning is limited, as there are only nine body systems. However, a variety of clinical signs are seen for any poisoning due to differences between individual and animal species. Some of these differences can be accounted for by anatomical and physiological differences between species, e.g. bracken fern contains a thiaminase which destroys the essential Vitamin B for the horse and rat but ruminants have microbes which synthesize their own Vitamin B and so don't require an exogenous source of the vitamin.

The course of the poisoning may be either acute or chronic. Acute poisoning is characterised by intense clinical symptoms, with a rapid course, often terminating with the animal's death. Chronic poisoning results from repeated exposure to low doses, or ingestion of a single dose of poison which is eliminated slowly from the body.

Debilitated animals are more susceptible to the action of poisons and drugs because their general resistance to adverse conditions is low and the mechanisms which assist in the detoxification and elimination of substances foreign to the body may be defective. Certain toxins do consistently affect specific systems of the body.

a. Nervous System

Toxicant induced seizures are usually generalised, bilaterally symmetrical and without local onset. The initiating cause of the seizures can seldom be determined by the type of the seizure alone. A toxin which produces signs of excitement is prognostically more favourable, than when paralytic symptoms are the result.

b. Alimentary System

Anatomical differences of the alimentary tract between species is very important in determining the course of the toxicity. Carnivores have a short, efficient digestive tract compared to herbivorous animals. Absorption from the alimentary tract of the dog is rapid and complete, so that a small amount of poison is likely to produce clinical signs. In ruminants, ingested poisons are diluted in the rumen and the ruminal microbes actively destroy some vegetable toxins. Malnutrition, parasitism and stress are important in lowering the resistance of the animal to poisons. The nature and quantity of feed ingested also influences the animal's response to gastrointestinal poisons.

The alimentary tract signs of diarrhoea, vomiting and constipation often occur in conjunction with the dysfunction of other organ systems.

c. Hepatotoxins

The liver is the major organ of drug metabolism and excretion. It has large reserves so that death usually occurs before the liver function is fatally impaired.

Liver function tests and clinical signs such as jaundice will not identify the toxic agent but will provide indirect information on the amount of damage caused to the liver. An animal exposed to a short-term or single hepatotoxic incident may regain full liver function if it survives the acute insult. The liver is usually swollen and oedematous following an acute chemical injury, conversely continued exposure to a hepatotoxin may result in fibrosis and cirrhosis, so that the liver becomes small and shrunken e.g. chronic facial eczema.

d. Nephrotoxins

Acute nephrosis results in similar clinical signs regardless of the cause, although these clinical signs may be complicated or obscured by the effects of other systems. The renal effects of a toxic agent may be apparent within hours following exposure, or renal failure may occur days later. Once the damage has occurred, healing may take weeks. Therapy must be aimed at determining the extent of the damage and keeping the patient alive until recovery can occur.

Urine examination may be helpful in detecting poisons and there are specific changes which may be seen (Table 1).

Table 1 Abnormal Colour of Urine

Poison	Colour	Mechanism	Comments
Chlorate Copper Doxrubicin- Kale Rape	Pink (on standing)	Haemoglobinuria	Due to excess haemolysis of red cells: This is basically prehepatic or haemolytic jaundice
Ibuprofen	Pink to red		
Phenols Creosote	Dark green (green)		Compare with biliverdin that arises from bilirubin on standing.
Proprofol	Green		
Chlorate Bracken fern Lupins	Pink	Haematuria	Due to damage of kidney or renal tract
Phenothiazine Myoglobin	Red		On exposure to air
Rifampin	Orange-red		Also fluids and skin
Acorns Rhubarb	Black-brown		If in horses check for azoturia
Phenacetin Picric acid and other aromatic nitro compounds.	Bright yellow	Excretion of metabolites	
Metronidazole	Yellow-brown		
Bilirubin	Red-gold colour imparted to froth on shaking		Produced by excessive excretion of bilirubin II which arises from obstructive or hepatic jaundice. In many cases due to plant or artificial poisons e.g. carbon tetrachloride, facial eczema

e. Blood

A variety of defects may be induced in the blood including hypoxia, haemolysis, aplasia, coagulopathy and hypocalcaemia. Agents acting directly on the lipid or protein structure of the erythrocyte may cause a massive haemolytic crisis with haemoglobinuria and haemoglobin nephrosis (e.g. arsine). Haemolysis can also result from the oxidative denaturation of haemoglobin with the formation of Heinz bodies leading to an increased fragility of the erythrocytes or to an increased rate of erythrocyte destruction. The resulting aplastic anaemia is usually accompanied by a granulocytopaenia and thrombocytopaenia.

The colour of the blood is important in the diagnosis of toxic compounds. (Table 2).

Table 2 Abnormal Colour of Blood

Poison	Colour	Mechanism
Nitrate/nitrite	Chocolate brown	Methaemoglobin
Copper	Chocolate brown	Methaemoglobin
Sodium chlorate	Chocolate brown	Methaemoglobin
Nitrous fumes (Silage)	Light brown	Methaemoglobin
Cyanide	Cherry red	Cytochrome oxidase inhibition
Carbon monoxide	Bright red	CO haemoglobin
Carbon dioxide	Dark red	Displaced oxygen

f. Respiratory System

The exposure to lung-damaging chemicals may occur by aerogenous or haematogenous routes. Toxicity is affected by the size of the inhaled particle and the route by which it is excreted (i.e. some volatile chemicals are concentrated at the pulmonary membranes during expiration). The response of the lung to toxicants generally includes irritation, necrosis, fibrosis or suppressed immunologic function. As with other systemic diseases the rate and depth of respiration may be significantly altered in a poisoned animal. The odour of the animal's breath, may indicate a likely toxin.

Table 3 Abnormal Breath Smell

Smell		Substance
Bitter almonds	-	hydrogen cyanide
	-	zinc phosphate
	-	arsenic trioxide
A smokey or choking smell	-	elementary phosphorus
Garlic or oyster smell	-	organophosphorus compounds

g. Cardiovascular System

A toxin can manifest certain effects on the cardiovascular system. These may be expressed, either directly or indirectly on the heart muscle, coronary vessels or the nervous innervation of the heart. The mechanisms of damage are complex and often interrelated. Both the rate and depth of heartbeats will be profoundly affected by most poisons.

3. Pathological Evidence

The necropsy of animals that have died or had to be destroyed contributes substantially to a diagnosis. The post mortem examination should be performed as soon as possible after the death of the animal. Euthanasia should never be carried out, until the animal has been carefully examined and the findings recorded.

The external features of the carcass, the colour of the mucous membranes and skin, and any discharges apparent from the body openings should be noted, then a careful and systematic examination of all the body systems is performed. When the abdominal cavity or stomach is opened, the odour, if any, should be noted and a careful search of the stomach contents should be made for recognisable or suspicious traces of poison or poisonous plants. Care should be taken not to spill the stomach contents as these may contain valuable material for analysis. Grey-white specks may indicate arsenic trioxide or flakes of paint for lead poisoning. Similarly the leaves of some plants can be easily recognised in the rumen e.g. tutu. The colour of the stomach contents may also be significant; see Table 4.

Table 4 The Colour of Stomach Contents

Colour		Poison
Green/blue	-	copper sulphate
Yellow, orange or green	-	chromic compounds
Black	-	acids or alkalis causing corrosion of the stomach lining

Toxic changes are less apparent in the rumen as the large volume of ingesta dilutes the toxin, and the rumen is lined with keratinised tissue. A similar procedure of examination should be followed for the small and large intestines.

Hepatic and renal lesions are frequently seen as these organs are the main routes of metabolism and excretion for most toxins. However the damage to renal and hepatic tissues is generally not specific.

The body musculature may show a peculiar colour, e.g. lead poisoning, or jaundice, or show signs of bruising and haemorrhage e.g. warfarin, bracken fern poisoning or sweet clover disease.

If the history indicates involvement of the nervous system, the brain and spinal cord should be examined and removed for further detailed examination.

a. Tissue samples for analysis and histopathology

i. Dispatch of Material:
Ideally the samples are dispatched to the laboratory as soon as possible. However, under certain circumstances, the samples need to be preserved. Refrigeration or freezing is usually suitable to delay putrefaction. Slicker pads should be placed with samples which are dispatched. However, if the dispatch is delayed, then chemical preservatives are necessary. Use ethyl alcohol, not aldehydes or denatured alcohols, and include a sample of the preservative as a control. Do not allow the samples preserved for histopathology to come in contact with those for chemical analysis.

The sample containers must be chemically inert, fluid tight and well labelled with the organ, case number, name and address of the sender and species. Each organ sample should be kept in a separate, well labelled container**.**

ii. Samples for Chemical Analysis:
Ensure that the correct samples for analysis are collected. The samples needed for toxicological analysis are liver, kidney, stomach contents, intestinal contents, blood and urine. At least 50gm of each organ should be sent or the whole organ if it weighs less. Approximately 10mls of blood, EDTA or heparin and as much urine as is available, is to be collected. The stomach may be tied off at each end and sent complete with its contents. When in doubt, it is always better to send too much rather than too little. In the case of small animals it is sometimes better to send the whole animal (particularly birds and neonates). Do not submit toxicological specimens known to, or likely to contain agents dangerous to laboratory staff, without contacting the laboratory for advice.

Table 5 Samples required for toxicological analysis

Sample Type	Amount	Condition	Examples
Feed or bait	500g or more	Plastic bag or glass jars – avoid spoilage by cooling	Anticoagulants, cyanide, heavy metal, herbicides, ionophores, nitrates, pesticides, salt
Plants	Whole, fresh or pressed specimen	Cool and dry in paper bag	Plant identification
Water	1 L	Preserving jar	Pesticides, pH, nitrate, salt, algae
Live Animal			
Whole blood	5-10 ml	EDTA anticoagulant	Anticoagulants, CBC, cholinesterase activity, lead, mercury, nitrate
Citrated blood	Tube filled to line	Citrate (Blue top tube)	Coagulation studies
Serum	5-10 ml	Spin and remove clot if delays possible Special tube for zinc	Nitrate, salt, zinc
Urine	5-50 ml	Plastic screw top pottle	Arsenic
Stomach or rumen contents	100g or more	Freeze	Cyanide, 1080
Biopsy specimens	Liver, kidney	Freeze, some fixed	Arsenic, copper, ragwort, cyanide, lead, phosphorus
Post-mortem			
Liver, kidney	200g	Freeze, some fixed	As above
Brain	Half	Half fresh, half fixed	Cholinesterase, organochlorine, salt
Fat	100g		Organochlorine, organophosphate

Table 6 Sample Submissions

Recommended by MAF for Specific poisons. (Bentley 1995)

Poison	Preferred Sample	Preferred Sample Weight
Alfatoxin	Feed	20 g
Alpha-chloralose	Ingesta	50 g
Anticoagulants*	Liver	10 g
Arsenic	Liver	20 g
Cyanide	Ingesta	50 g
Heavy Metals (other)	Kidney whole and liver	10 g
Lead	Kidney whole and blood	10 g, 5 ml
Mercury	Kidney whole, feeds	10 g
Mesural (methiocarb)	Ingesta	20 g
Metaldehyde	Ingesta	50 g
Organochlorines**	Fat	20 g
Organophosphates***	Ingesta/Liver/Fat/Blood (EDTA)	20 g
Paraquat/Diquat	Kidney whole, feeds	50 g
Pindone	Liver	20 g
Phosphorus	Ingesta	100 g
Strychnine	Ingesta	20 g
1080 (fluoroacetate)	Ingesta	20 g
Trace elements (Cu, Se)	Liver/Kidney	10 g

* Test detects six coumarin-based anticoagulants, brodifacoum, bromadiolone, coumatetrayl (Racumin), difenacoum (Ratak), flucoumafen (Storm) and warfarin.

** The organochlorine test can detect several organochlorines

*** The organophosphate test can detect most organophosphates.

b. Tissue Samples for Histopathology

An histopathological examination is indicated for any organs which are grossly abnormal or which are suspected to be diseased. In most instances liver, kidney, lung and brain sections should be sent.

Samples for histopathology should be collected as early as possible and placed in fluid tight, correctly labelled containers in 10% formalin (10% formalin is nine volumes of water to one volume of commercial formalin). Use a volume of formalin that is 10 times greater than the volume of tissue to assure adequate fixation.

i. The Central Nervous System:
The brain requires special handling because lesions and/or infections are often localised to specific regions. Aim to remove the brain whole, then divide it longitudinally (in the midline). Fix one half and submit the other half unpreserved for chemical analysis. The cerebral hemispheres alone are usually of little value, and the cerebellum and brainstem should always be included. In small animals the spinal cord can be obtained by removing the dorsal half of the vertebrae. In large animals, the entire spinal column (divided into cervical, thoracic and lumbar segments) should be submitted to the laboratory.

4. Analytical Evidence

The final proof of poisoning lies in the detection of a significant quantity of the toxic agent in the body of an animal. However, toxicological analysis of tissues is not always easy to perform and it is often not available at a reasonable cost. For many toxins, particularly the plant toxins, there are no reliable chemical tests.

To test for a single poison or group of poisons is usually practicable, but to make a generalised search for a toxin is not. The function of a chemical analysis is to provide evidence to confirm a tentative diagnosis, and it is the responsibility of the veterinarian to suggest a likely toxin. To aid the laboratory in their analyses, a full clinical history, necropsy findings and details of any medicines given, should be sent with all the samples. Information on certain therapeutic compounds which may interfere with the analysis should be given. These can be erroneously identified as the toxin. If litigation is a possibility, then the laboratory should be warned, samples carefully identified and properly labelled. Meticulous records must be kept.

Try to send a sample of the suspected toxic material. This is particularly helpful with organophosphates and other poisonings where standards for comparison may not be readily available to the laboratory. If this is a plant, send the leaves, flowers, fruit or roots.

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Hill, F. (2002). Laboratory diagnosis of poisonings in production animals. Proc. of the 32nd Seminar Sheep & Beef Cattle Veterinarians NZVA. 1-18.

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The Treatment of Poisoning

All cases of poisoning should be considered as emergencies and treatment should be started as soon as possible. The initial treatment will be aimed at stabilizing the patient until the toxic agent can be identified and antidotal therapy may be given. In general treatment is directed along three lines which are as follows:

1. Remove the source of poison and deal with any life-threatening conditions.

2. Limit the further absorption of the poison and hasten its elimination from the patient's body. In other words thoroughly decontaminate the animal.

3. Reduce the effects of the poison by both symptomatic and supportive therapy and if the poison has been identified apply specific antidotes if they are available.

The preliminary advice given to the client at the initial contact is very important and often has a profound effect on the success of any subsequent treatment.

1. Removal from the Source of Poison and Life Threatening Conditions

Removal of the animal from the source of poison, if it is known, is most important. In the case of grazing animals and animals which have died in a certain paddock, the rest of the flock or herd should be quickly moved to a new location. Such a move may be only temporary for example, in nitrate/nitrite poisoning the toxic level of some pasture species is only high for a brief period. Alternatively if the source of poison is not known then time is gained while the environment is thoroughly searched for the toxic plants or material. The provision of fresh water in such instances is also important as many toxicological conditions cause severe dehydration of the affected animals.

In the case of pets or small animals the client should be instructed to keep the animal quiet and warm. In some cases instructions such as muzzling a large dog may be necessary to avoid the owner or other onlookers from being hurt. (Many poisoned animals have violent nervous signs which are quite out of character with the animals' usual demeanour).

2. Limiting the Absorption of the Poison

If the poison is on the skin e.g. insecticides or corrosive chemicals, the client should be instructed to wash the animal(s) with copious amounts of warm water. It is best not to use soap or detergents as these may facilitate further absorption of the poison. In some instances it would be wise to warn owners to take precautions themselves, by wearing protective clothing, in particular gloves.

a. In the case of recently ingested poisons, the owner can attempt to induce vomiting, but before doing so the veterinarian should make the following points.

i. If the chemical was of a caustic or corrosive nature, induced vomiting may cause further oral or oesophageal damage. A careful look at the mouth or paws of a cat or dog may indicate corrosive lesions. In the case of suspected acid contact or ingestion, advise the owner to give milk or water.

ii. Forced vomiting should never be recommended if the patient is severely depressed, comatose, or having intermittent seizures or convulsions.

b. To induce vomiting the owner may use one of the following (It is important to recognise that no treatment is totally satisfactory for emptying the stomach):

i. 1-3 teaspoons of table salt in warm water and given orally. This is not very effective and can cause hypernatraemia. Use as a last resort only if no other emetics are available in the home.

ii. 1-3 teaspoons for small animals or 1-3 ml/kg (1 teaspoon = 5 ml) of 3% hydrogen peroxide orally, repeat at 10 minute intervals up to three times. Do not confuse with concentrated hydrogen peroxide used as a bleaching agent.

iii. Dry Mustard 1-4 teaspoons in 250 mls (cup) of water.

iv. A crystal of washing soda (sodium carbonate) placed on the back of the tongue, or a 1% solution of copper or zinc sulphate (10-30ml for dogs, 3-10ml for cats) are all procedures which may be recommended in an emergency. As little as 40 mg of copper sulphate will induce emesis in the dog.

v. Liquid dishwashing detergent (but not laundry or electric dishwashing detergents) are generally effective. The dose is 3 tablespoons in 250 ml of water, given at 10 ml/kg or 2 teaspoons/kg.

Of these home remedies the crystal of washing soda and copper and zinc sulphate are the most effective. The amount of food in the stomach affects the success of the emetic. In the case of a low volume, highly toxic compound feeding just before giving the emetic may be beneficial. Avoid fatty foods that may enhance the absorption of lipid soluble agents.

The animal should be given access to fresh water, egg white and milk. The latter two materials are useful adsorbents, particularly for corrosive materials. If the dog or cat does vomit and the vomitus can be collected in a suitable container the owner should be asked to bring this to the clinic for further analysis.

3. Veterinary Examination and Treatment

With farm animals the degree of medication and emergency treatment possible may be limited by the number of animals and the ability of veterinarian and owner to deal with so many animals quickly. Specific instructions for each toxicosis of farm animals is given, where applicable, in later sections. The following recommendations generally apply to pet or small animals. However many of the principles can be used in farm animal therapy as well. The management of the poisoning should be done in an organised sequence: first, stabilise the animal's vital signs; second, clinically evaluate the animal; third, prevent continued exposure to the poison; fourth, administer an antidote if available; fifth, facilitate removal of the poison and sixth, supportive therapy and observation. It is important to remember to treat the patient not the poison.

When the animal is first seen by the veterinarian, the initial treatment is aimed at managing any life-threatening conditions regardless of whether or not the poison is known. An

immediate examination of vital systems should be made and emergency therapy begun according to the ABCD mnemonic i.e. airways, breathing, cardiac function and drugs.

a. Examination of the patient

i. Ensure the animal has a patent airway and if necessary assist respiration by the administration of oxygen. Prevent the aspiration of vomitus. Anticonvulsant therapy may also be necessary at this stage and may include the use of diazepam (Valium) which should be given slowly and intravenously (dogs 0.5mg/kg; cats 0.5 mg/kg).

Alternatively, sodium pentobarbital may also be given intravenously to effect. The amount given will vary according to the individual and the effect produced. The dose used is calculated on the basis of 13 mg/kg bodyweight. From one third to half the dose may be given over a period of 10 seconds and the remainder should be given slowly over a period of several minutes. The depth of anaesthesia must be carefully checked and in the case of very sick animals the dose may need to be reduced. In some cases phenobarbital (6 mg/kg) will be effective in controlling seizures. Methocarbamol (Robaxin®) (40-200 mg/kg IV to effect) is useful to relax skeletal muscle (e.g. strychnine).

ii. Where signs of shock or dehydration are apparent, intravenous fluids should be administered. Generally speaking, give balanced electrolyte solutions or saline to replace deficits, provide for ongoing losses and maintenance requirements. Excess fluid administration is likely to result in pulmonary oedema while dehydration can be assessed in most animals by skin turgor or tenting. Blood samples for electrolyte, glucose and serum chemistry should be taken before fluids are given. Acid-base balance should be assessed and treated accordingly.

iii. Every attempt should be made to maintain the animal at near normal body temperature. If the animal is in hypothermia, blankets and a **WARM** hot water bottle should be used. If the patient is conscious, warm milk or water may be given by mouth. If the animal is in hyperthermia, the temperature should be monitored and if it does not decrease (particularly once seizures are controlled) then a cold bath should be given.

iv. The patient's fluid balance should be adjusted according to acid-base and electrolyte estimations in order that there is an adequate output of urine. Sodium bicarbonate (0.5-2.0 mEq/kg every 4 hours IV) for metabolic acidosis or to trap acidic drugs in the urine (e.g. aspirin).

4. Preventing Further Absorption of the Toxic Material and Hastening Elimination

Once the life-threatening situations are controlled, attention should be paid to the prevention of further absorption of the toxin, enhanced excretion and the application of specific or non-specific antidotal therapy.

In the case of chemicals with which you are unfamiliar either a textbook or the poison control centre should be consulted.

a. The following is a suggested procedure to follow:

i. If the route of contact was dermal ensure that the animal either has been well washed with tepid water or see that thorough washing is carried out. Mild shampoo or liquid dishwashing detergent may be used.

ii. If the route of contact was oral then in the dog, cat and pig an emetic may be given. Emetics are contraindicated in rodents, rabbits and horses because they cannot vomit safely. Emetics are most effective if given within 4 hours of the poison being ingested. Apomorphine is usually recommended, but it may add to the toxicity of the poison by causing respiratory depression and protracted vomiting. Crush a tablet of apomorphine, add to a small amount of sterile saline and administer subconjunctivally for a dog. After the dog has vomited rinse the eye to remove the apomorphine. Alternatively a dose of 0.1 mg/kg SC (3-6mg) may be administered. The cat is less sensitive to apomorphine than the dog and the high dose rates recommended make its application to this species unsuitable. Apomorphine should not be used in cases of severe CNS depression or when the animal is seizuring. The undesirable signs produced by apomorphine may be effectively controlled afterwards by the intravenous administration of an appropriate narcotic antagonist (e.g. naloxone (Narcan) 0.04 mg/kg; levallorphan (Lorfan) 0.02 mg/kg or nalorphine (Nalline) 0.01mg/kg.

Alternative drugs which may be used as emetics are xylazine (Rompun 2% solution) (cat 0.1-0.2 ml/kg; dog 0.5-1.5ml/10kg SC or IM) and morphine, although the latter is likely to be less available in most veterinary practices. Yohimbine (0.1 mg/kg IV) is used to reverse respiratory depression resulting from xylazine use.

	Cat	**Dog**
xylazine	1.1 mg/kg	1.1 mg/kg

Following forced emesis ensure that the animal does not inhale its vomitus as this may lead to the development of an aspiration pneumonia. Induced vomiting is contraindicated in cases of poisoning by barbiturates, kerosene, and corrosive substances.

iii. Gastric lavage may be used to remove ingested poison if the animal is either comatose or has been anaesthetised. Gastric lavage is most effective when performed within 1-2 hours of ingestion. The procedure is as follows: firstly insert an endotracheal tube and inflate the cuff; next insert the gastric tube, using one with as large a diameter as possible and by the use of suction or gravity drain as much of the gastric contents off as possible. The patient's head should be kept lowered slightly during the procedure. Take great care when inserting the stomach tube as penetration of the oesophagus or stomach wall may occur if they have been damaged by the poison.

One hundred millilitres to 200ml of warm tap water (10 ml/kg) should be instilled repeatedly and drained off until all the stomach content has been removed and the lavage fluid is clear. Activated charcoal (5-10 ml/kg) can be used in the final flushings. Mix 1 gram of activated charcoal in 5 mls of water. Cattle should receive 1 kg/500kg of body weight. The constipating effect of activated charcoal should be countered by using sorbitol (1-4 gm/kg) or other laxative with the first dose of activated charcoal (Table 7). Repeated doses of laxatives are contraindicated.

Table 7 Cathartics (laxatives) doses

	Horse	Cow	Sheep and Goats	Pig	Dog	Cat
Sorbitol (70%)					1-4 gm/kg	1-4 gm/kg
Magnesium sulphate (Epsom salt)	100-200 grams	100-200 grams	25-125 grams	25-125 grams	0.5-1 gm/kg	2-5 gm only
Activated charcoal and sorbitol (Carbosorb S®)					1 gm/kg	1 gm/kg
Sodium sulphate (Glaubers salt)	250-375 grams	500-750 grams	60 grams	30-60 grams	5-25 grams	2-5 grams

5. Adsorbents

Following forced vomiting or gastric lavage a further decontamination should be given. Universal antidotes containing activated charcoal, magnesium oxide, kaolin and tannic acid (tea does not contain tannic acid) are no longer considered therapeutically valid. Activated charcoal binds to part of the magnesium oxide and tannic acid diminishing its adsorptive properties. Administered alone, activated charcoal (1-4 gm/kg) and kaolin (15 gm/kg) will adsorb most poisons, while tannic acid ($C_{14}H_{10}O_9$) will precipitate any alkaloid or heavy metal which may remain in the stomach. Tannates which are formed are insoluble. Light magnesium oxide neutralises acids and has a laxative effect.

Catechu, a powerful astringent plant extract, is found in antidiarrhoeal remedies.

Activated charcoal is a finely divided, black powder that is sparingly soluble in water. It is prepared by pyrolysis of organic matter. The charcoal is activated by exposing it to oxidation with steam or oxygen at temperatures over 600°C. Activated charcoal has a surface area of about 1,000 M^2 or greater. Activated charcoal will adsorb materials from water and air if mixed in water and allowed to stand. It adsorbs many but not all poisons (see Table 8).

Table 8 Compounds POORLY or NOT Adsorbed by Activated Charcoal

Acids	Gold
Alcohol	Lithium salts
Alkalis	Malathion
Boric acid	Mercury
Cyanide	Mineral acids
DDT	N-methyl carbamate
Electrolytes	Petroleum
Ethylene glycol	Potassium
Ferrous sulphate (Iron)	Water insoluble compounds
Fluoride	

6. Ion Exchange Resins

An anion exchange compound used to bind toxins is cholestyramine resin (Questran). Cholestyramine binds with lipoproteins and bile acids thus preventing intestinal absorption that occurs via these systems. Cholestyramine can interrupt the enterohepatic recirculation of compounds excreted via the bile. Examples of compounds that the resin will bind with are phenobarbital, propranolol, tetracycline, penicillin G, digoxin, thyroxin, phenylbutazone, some pesticides, any highly lipophilic compound, heat stable *Escherichia coli* enterotoxin and warfarin. The recommended dosage for animals is 50-75 mg/kg PO. Fluid therapy may be required as hydration status is important when cholestyramine resin is used. Questran contains 4 grams of cholestyramine with aspartame and orange flavouring to be mixed with water, milk or fruit juice.

The potential side effects of cholestyramine are nausea, hypoproteinaemia, constipation, steatorrhoea and the loss of fat-soluble vitamins. In humans the reported side effects include irritation to the tongue and perianal area, muscle and joint pain, headache and dizziness.

7. Demulcents

Demulcents may reduce gastrointestinal tract irritation and compounds which are suggested include; a mixture of egg white, sugar and milk, linseed tea and oatmeal gruel. Diluted egg whites (4-6 to 1000ml of tepid water) or whole milk may be given. These should be followed by an enema and then a cathartic particularly in alkali poisoning because some compounds are soluble in excess albumin.

8. Large Animals and Ruminant Animals

It is impossible to wash out the stomachs of large animals and ruminants. The only effective method of emptying the stomach in ruminants is by rumenotomy. If the ruminal contents are removed it is essential that they are replaced by suitable sloppy material. A good mixture is chaff mixed with bran and well crushed oats, scalded with boiling water but brought back to body temperature before dosing. Re-establishment of the bacterial flora in the rumen is ensured by dosing with one or two cuds from a healthy animal.

9. Colonic Lavage and Osmotic Cathartics

These procedures aim at hastening the elimination of any ingested and absorbed toxin.

a. Colonic lavage

The enema should consist of warm water and activated charcoal, or warm water and a soft soap (e.g. sunlight soap). The bowel is evacuated by gravity and the enema dose (approximately 200-500ml) should be given several times.

b. Cathartics

The cathartic should be administered by stomach tube, following gastric lavage. Sodium sulphate is preferred to magnesium sulphate (Epsom salts) particularly when mixed with activated charcoal. The use of magnesium sulphate may produce depression of the central nervous system and release of toxin from charcoal is less likely when sodium sulphate is used. Mineral oils are useful if lipid soluble toxicants are involved. Mineral oil is inert and unlikely to be absorbed whereas vegetable oils are readily absorbed and are therefore contraindicated. Oil should be followed by a saline cathartic given 30 minutes afterwards. (See Table 7).

10. Hastening the Elimination of Absorbed Toxicants

a. Renal elimination

Absorbed toxicants are generally excreted via the kidneys, although other routes such as bile, faeces, lung and other body secretions may be involved.

The urinary excretion of toxicants may be enhanced by the use of diuretics or by altering the pH of the urine. The use of diuretics to enhance urinary excretion of toxicants requires adequate renal function and hydration of the affected animal. Monitoring urine output is essential. The diuretics of choice are mannitol (2g/kg/hour) and furosemide (5mg/kg every 6-8 hours). Alteration of the urinary pH to increase the excretion of toxicants is a common technique and relies on the fact that ionised compounds do not readily cross cell membranes, and therefore are not reabsorbed. Generally speaking, acidic compounds (e.g. acetylsalicylic acid) and some barbiturates are largely ionised in alkaline urine and alkaline compounds tend to remain ionised in acidic urine.

Agents which acidify urine include ammonium chloride (200 mg/kg/day in divided doses) and ethylenediamine dihydrochloride (Chlorethamine 1 to 2 tablets given three times daily, for an averaged sized dog). Sodium bicarbonate may be used as an alkalinising agent; in an emergency give 1-2 mEq/kg IV.

b. Respiratory tract

Ensure adequate ventilation and administer oxygen as necessary.

c. Gastrointestinal tract

Continue the use of cathartics and colonic lavage with the oral administration of activated charcoal.

d. Liver

Maintain fluid therapy to favour adequate perfusion of the liver. Also the use of antibiotics may be considered to protect against bacterial invasion of the liver and other parenchymatous organs.

11. Antidotal Therapy

Specific treatment of poisoning can only be instituted when the identity of the toxin is known, so that the appropriate antidote can be given. There are few specific antidotes and caution is required in their use, as many of these are themselves toxic.

12. Chelation Therapy

Metals can form complexes with organic molecules known as chelates. This is a reversible interaction that can alter absorption, transport and excretion of metals. A chelator may bind to several other metals in the body such as calcium resulting in a hypocalcaemia (e.g. ethylenediaminetetraacetic acid (EDTA)). There is no ideal chelator. Each chelator has side effects, contraindications and precautions for use. Chelation may cause the animal's condition to worsen, particularly if the source of the metal is not removed, e.g. metal objects in the gastrointestinal tract. A list of available chelators are listed in Table 9.

Table 9 Metal Chelators

Metal	BAL	CaEDTA versenate	Penicill-amine	DMSA	DMPS	Thioctic acid	N Acetyl cysteine	Other
Arsenic	X			X	X	X	X	
Copper			X	X	X			Molybdenum
Fluorine								Calcium gluconate, Al or Ca
Iron			X					deferoxamine
Lead	X	X	X	X	X			
Mercury	X*		X*	X*	X*			
Phosphorus								Copper sulphate or potassium permanganate
Selenium							X	
Thallium								Prussian blue or K ferric furocyanide
Zinc		X	X					

* Depends on the form of mercury, chronicity and renal function. See the chapter on mercury (Page 73).

British Anti-Lewisite (BAL) was designed to bind with arsenical gas but will also chelate lead. BAL is useful to treat acute or chronic poisoning by organic and inorganic arsenicals and protects against mercury-induced renal injury. For mercury it is not considered effective unless given prior to the onset of clinical signs. It is not recommended for cadmium toxicity as it may enhance renal damage due to partial dissociation in the urine. BAL is not recommended for iron or selenium poisoning. Toxic side effects of BAL use include nephrotoxicity, increased blood pressure, tachycardia, lacrimation, nausea, vomiting, muscle cramps, paresthesias, restlessness, tremors, coma and death. Injections are painful.

Dimercaptosuccinic acid (DMSA) and 2,3-dimercapto-1-propanesulfonic acid (DMPS) are water-soluble analogues of dimercaprol (BAL). Compared to BAL, DMSA and DMPS are less toxic and effective when given orally. Adverse effects caused by DMPS in dogs include muscle tremors, tachycardia, dyspnoea, vomiting and defaecation. DMSA and DMPS will chelate arsenic, copper, lead and mercury.

Calcium disodium edetate (CaEDTA), also known as calcium disodium versenate, will chelate metals that have a higher binding affinity than calcium^{2+}, e.g. lead, iron, nickel, zinc, manganese, beryllium and copper. CaEDTA is used to prevent binding with calcium resulting in hypocalcaemia. CaEDTA does not readily penetrate cells but complexes with circulating metal ions. It is not recommended for oral use as it may chelate dietary metals and aid absorption. Toxicity of EDTA limits its usefulness. EDTA may cause severe proximal nephron degeneration. Other effects reported include vomiting and diarrhoea (dogs), fever, dermatitis and nasal congestion.

Penicillamine is obtained by the hydrolysis of penicillin, and only the D-isomer is recommended for use. It is given orally and is well absorbed. It effectively chelates copper, iron, mercury, zinc and lead and promotes their excretion in the urine. The drug is used for copper storage-associated hepatopathies in dogs and lead poisoning. An adverse effect associated with penicillamine is vomiting.

Desferrioxamine mesylate (Desferal®) is a good chelating agent for iron toxicity. The drug is given intravenously or intramuscularly. Desferrioxamine is toxic and should not be used unless the severity of the iron toxicity warrants its use. Potential problems associated with human use are allergic reactions, pain at the injection site and gastrointestinal distress.

13. Treatment of Convulsions

Convulsions are very distressing for the owner and dangerous in the case of large animals. Depending on the cause, they can also quickly cause serious damage to the animal's CNS. They should be treated as an emergency.

In general, benzodiazepines (diazepam) should be given intravenously immediately after a quick preliminary assessment; this will allow safer handling of the animal and some time for further assessment and organisation of the definitive treatment. Remember to secure the airway and prevent inhalation of vomit. Placing an IV catheter is essential.

a. Benzodiazepines

Benzodiazepines bind to $GABA_A$ receptors to increase opening, which causes an inflow of chloride ions into the neurone and hyperpolarisation. Benzodiazepines will potentiate other drugs with the same mechanism of action, i.e., most other anaesthetics. They have anticonvulsant, sedative and muscle relaxing effects, and only produce respiratory depression at very high doses.

i. Diazepam

Initially diazepam should be given at 0.5 - 2 (dogs and cats) - 5 (adult horses and cattle) - 9 (foals) mg/kg. Give the lowest dose by slow IV injection, followed by more slow injections to effect. The dose is not critical as diazepam is very safe.

In dogs, IV injections are best made into the lateral saphenous vein, to avoid accidentally getting bitten. In large animals, the jugular vein is probably best approached from behind the laterally recumbent animal by leaning over its neck to avoid getting kicked. This procedure is much easier if an assistant holds the head down.

If it is not possible to find a vein, diazepam solutions (Pamlin, many human products) can be given IM. Diazepam emulsions (Diazemuls) should not be given IM. As a last resort, both can be given per rectum, but absorption is variable.

Diazepam only lasts a short time, usually about 20 minutes. A second dose can be given, or the animal can be given an IV infusion. A maximum of 80mg/L in 5% dextrose should be used, and the mixture used within 6 hours as diazepam can stick to the plastic in infusion bags and giving sets. Animals rapidly become tolerant to diazepam and other drugs usually have to be used after the initial control of convulsions with diazepam.

ii. Midazolam

Midazolam (Hypnovel) is very similar to diazepam, but is water soluble which overcomes problems with the vehicle in injections. It is short acting, and an IV infusion is likely to be needed after the initial IV injection.

Initial dose (all species) 100 - 200μg/kg IV. This is only likely to last about 10 minutes.

iii. Clonazepam

Clonazepam (Rivotril) is often used in people for treating convulsions. Experience in animals is limited.

Dose for dogs is 50 - 200μg/kg IV

In the very unlikely event of benzodiazepine overdose causing respiratory depression, the antagonist **flumazenil** (Anexate) can be given at 100μg/kg IV every minute until the effects are reversed. Flumazenil is **very** expensive.

b. Pentobarbitone

If the animal starts to convulse again as the diazepam wears off, pentobarbitone is usually given.

Dose in all species is 10 - 15mg/kg slowly IV. It has a much slower onset of action than modern anaesthetics, so top up doses to effect should not be given until 2 - 3 minutes after the first dose.

Pentobarbitone is a barbiturate, which acts on $GABA_A$ receptors in a similar way to the benzodiazepines. It is potentiated by any remaining diazepam, so dosing must be to effect. It is likely to cause significant respiratory depression and the animal should be intubated.

Anaesthetic pentobarbitone should be used; euthanasia solutions are not sterile.

Phenobarbitone

Phenobarbitone is more anticonvulsant than other barbiturates, but IV solutions are rarely available when needed.

Dose 3 - 6 (- 20) mg/kg slow IV. Onset takes about 20 minutes, so small doses every 20 minutes until an effect is seen is the best way of giving it. Diazepam or pentobarbitone may have to be given until it takes effect.

Overdose is likely to cause anaesthesia with respiratory depression. If this occurs, the animal should be intubated and ventilated until the effects wear off. This may take some time.

c. Other Anaesthetics

If pentobarbitone or phenobarbitone are not available, anaesthesia may be induced with **thiopentone** and maintained with **halothane**. Anaesthesia should be kept as light as possible.

d. Other Drugs

If the muscle rigidity arises from the spinal cord rather than the brain, drugs which act at this level to cause muscle relaxation are sometimes used.

Methocarbamol was useful but is not currently licensed in New Zealand. If it can be obtained, the dose is 150mg/kg slowly IV for dogs, followed by 75mg/kg IV as necessary. For cats, 55 - 220mg/kg IV to effect. For horses, 22 - 55mg/kg to effect. For cattle, 110mg/kg to effect.

Guaiphenesin (glycerol guaiacolate (ether), GG) has been used but causes haemolysis, particularly in dogs. Its main advantage is that it is relatively cheap if the animal requires several days of treatment. Dose: dogs, 44 - 110mg/kg IV to effect, horse and cattle, 66 - 132mg/kg IV to effect, pigs, 44 - 88mg/kg IV. There is no information on withholding times. Avoid if possible.

Acepromazine has been advocated for treating convulsions, but it lowers the threshold for convulsions and can cause a variety of dyskinesias which resemble convulsions. It should not be used.

Xylazine, and probably other alpha$_2$ agonists, can have some anticonvulsant effects; however, xylazine can also be proconvulsive and can antagonise the effects of benzodiazepines and barbiturates. Its use should be avoided.

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