2: Poisonings: Investigation & Management

> *Dans les champs de l'observation le hasard ne favorise que les espirits prepares.* (Where observation is concerned, chance favours only the prepared mind; paraphrased as **Fortune favours the prepared mind**)
>
> Louis Pasteur (1822-1895) Address given on the inauguration of the Faculty of Science, University of Lille, 7 December 1854

☑ Is it a poisoning? *What flags poisoning as a possible diagnosis?*

Signs and circumstances suggesting poisoning as one differential diagnosis in a case are

- simultaneous onset of illness of similar severity in several animals
- illness closely following medication or a change of feed, locality or weather
- sudden death: see Radostits *et al.* 1994 or 2000 for differentiation in farm animals
- acute liver necrosis
- photosensitisation

Many other signs in poisonings are shared with infectious, genetic, metabolic or nutritional diseases, e.g. vomiting, diarrhoea or nervous dysfunction.

References:

Radostits *et al.* (1994) *Veterinary Medicine.* 8th edition, pp. 64-66 or
Radostits *et al.* (2000) *Veterinary Medicine.* 9th edition, pp.75-77.

How frequent is poisoning of animals compared with other diseases?

Data to answer this question are scanty. Clearly, the incidence of poisoning will vary with animal species, geographical location and time.

It is interesting to note that the first scientific paper ever published in the *Australian Veterinary Journal* (then, briefly, *The Journal of the Australian Veterinary Association*) described deafness in dogs and cats due to poisoning by therapeutic doses of the anthelmintic oil of chenopodium if a purgative was not given simultaneously (Clunies Ross 1925).

Dogs (and Cats)

A study of necropsy findings from 1933 dogs which died suddenly and unexpectedly during the 10 years 1989-1999 in Saskatoon, Canada, and were examined at the Western College of Veterinary Medicine revealed that toxicity (mostly due to strychnine poisoning, but including one case of CO poisoning and some possible anticoagulant rodenticide poisonings) was the second most likely diagnosis and accounted for 15-20% of cases (Olsen & Allen 2000). Not surprisingly, the most likely cause of death was heart disease (>20% of cases) and no diagnosis was reached in 13% of cases. A parallel study of necropsy records of sudden death in cats revealed no recognised poisonings (Olsen & Allen 2001). A study of 330 cases of sudden and unexpected death in dogs in Germany (Wanke 1988) revealed 83 cases (25%) due to proven or suspected poisoning (organophosphorus compounds, strychnine, metaldehyde, chlorinated hydrocarbons, heavy metals).

Cattle

The proportion of cattle deaths diagnosed annually by the Queensland DPI's Animal Research Institute diagnostic service (ARI) that were due to plant poisoning in the years 1972-1981 ranged from 5 to 23% (mean 12%). The annual total of cattle deaths investigated by ARI in this period ranged from 1630 to 4321 (mean 2369), representing 0.4 to 1.0% of cattle deaths in Queensland recorded from returns to the Australian Bureau of Statistics. Bear in mind that submissions to diagnostic laboratories are not accurately representative of field mortalities and exclude many cases of well-recognised conditions such as poisoning by *Lantana camara, Pteridium esculentum* and *Pimelea* spp. (McKenzie 1985).

References:

Clunies Ross I (1925) Toxic symptoms following the administration of Ol: Chenopodium. *J. Aust. Vet. Assoc.* **1**:7-8.
McKenzie RA (1985) The cost of cattle deaths from toxic plants in Queensland, 1972-1981. In Seawright AA, Hegarty MP, James LF, Keeler RF (eds) *Plant Toxicology.* Queensland Poisonous Plants Committee, Brisbane. pp.14-23.
Olsen TF, Allen AL (2000) Causes of sudden and unexpected death in dogs: a 10-year retrospective study. *Can. Vet. J.* **41**:873-875.

Olsen TF, Allen AL (2001) Causes of sudden and unexpected death in cats: a 10-year retrospective study. *Can. Vet. J.* **42**:61-62.
Wanke R (1988) [Sudden and unexpected death in the dog. A review of more than 330 cases based on *post mortem* findings.] *Kleintierpraxis* **33**:5-10. [in German, English abstract]

What are the most common poisonings in veterinary practice?

The absolute list and relative ranking of prominent poisoning causes in domestic and wild animals will vary with **animal species**, **geographical location** and **time**. Published data for Australia are scanty.

Frequently reported poisonings of companion animals

Australia

Dogs

Brisbane 1970-81: lead >> strychnine >> organophosphorus insecticides > anticoagulant rodenticides > molluscicides > organochlorine insecticides (Prescott 1983)

Melbourne 1971-83: molluscicides > snake bite > anticoagulant rodenticides > lead > organophosphorus insecticides > strychnine (Studdert 1985)

Perth 1978-90: molluscicides > snake bite > anticoagulant rodenticides > plants > insecticides > strychnine, phenols > lead (Robertson *et al.* 1992)

Rural WA 1978-90: insecticides > anticoagulant rodenticides > molluscicides > strychnine > arsenic > 1080 (Robertson *et al.* 1992a,b)

All states 1996: molluscicides, rodenticides, strychnine, fluoroacetate (RSPCA survey of veterinarians)

Cats

Brisbane 1970-81: organophosphorus insecticides > lead, anticoagulant rodenticides > organochlorine insecticides (Prescott 1983)

Melbourne 1971-83: snake bite >>> organophosphorus insecticides > molluscicides > miscellaneous household products > anticoagulant rodenticides, medications > organochlorine insecticides (Studdert 1985)

Perth 1978-90: snake bite, molluscicides > organophosphate insecticides > anticoagulant rodenticides (Robertson *et al.* 1992a,b)

Rural WA 1978-90: anticoagulant rodenticides > organophosphorus insecticides (Robertson *et al.* 1992a,b)

North America

Dogs: rodenticides > human medicines > insecticides > plants (Bistner & Ford 1995)

Cats: insecticides > plants > human medicines > rodenticides > veterinary medicines (Bistner & Ford 1995)

See also Murphy (1996) for a list of common intoxications in North America by organ system and toxin type.

United Kingdom

Most frequent enquiries to Veterinary Poisons Information Service 1993-1998: NSAIDs (including ibuprofen, paracetamol, diclofenac), anticoagulant rodenticides, metaldehyde, salbutamol (Ventolin®), borax, permethrin (cats), chocolate, glyphosate, paraquat, fertilizers, alphachloralose; (most frequent fatal outcomes): agent unknown, metaldehyde, paraquat, anticoagulant rodenticides, cyanobacteria (blue-green algae) (Campbell 1999)

References:

Bistner SI, Ford RB (1995) *Kirk and Bistner's Handbook of Veterinary Procedures & Emergency Treatment*. 6th edition. WB Saunders Co., Philadelphia.
Campbell A (1999) Common causes of poisoning in small animals. *In Practice* **21**:244-249.
Murphy MJ (1996) *A Field Guide to Common Animal Poisons.* Iowa State University Press, Ames, Iowa. pp.2-6.
Prescott CW (1983) Clinical findings in dogs and cats with lead poisoning. *Aust. Vet. J.* **60**:270-271.
Robertson ID *et al.* (1992a) *Aust. Vet. Practit.* **22**:78
Robertson ID *et al.* (1992b) *Aust. Vet. J.* **69**:194
Studdert VP (1985) Incidence of poisoning in dogs and cats in Melbourne. *Aust. Vet. J.* **62**:133-135.

💣☑ *Managing a Poisoning Emergency in an Individual Animal*

The scope of the task

Beyond the most common toxins, there are numerous other potentially-toxic compounds, both natural and industrial, available to animals.

To deal effectively with poisoning emergencies, a veterinarian must

- **master the general management of intoxications** (this section), and
- **consult specialist centres for specific information and advice about less-common intoxicants** (see the section on *Information Sources for Veterinary Toxicology in Australia*)

Common scenarios faced by the veterinarian

In decreasing order of frequency. An animal may be presented with

- unknown history & range of signs suggesting toxicity
- signs of intoxication by a known poison about which you may know little or for which an antidote is not readily available
- signs of intoxication by a known poison with which you are familiar and for which there is an antidote (rare)

First contact: dealing with clients over the telephone

"My dog/cat is acting sick and I think he/she has been poisoned!"

This process has been termed "telephone triage" (Drobatz 1994). The term derives from military medicine and means the sorting of battlefield casualties according to the urgency of the treatment they need.

The aims of the telephone conversation from the veterinarian's viewpoint are to

- **decide if the patient needs veterinary examination**
- **decide and advise what the client can do for the patient**
- **calm the client**. If they are very upset, advise them to seek aid from friends or relatives to transport them and the patient to the veterinary clinic safely.

Range finding: collect a history

Questions to ask during the telephone conversation (modified from Drobatz 1994):

About the patient:

- What is the patient's species, age, breed, sex and approximate weight?
- What clinical signs are being seen?
    - When did they start?
    - Are they getting worse, better, or staying the same?
    - When was the suspected exposure to the toxin?
- Why do you think your animal has been poisoned?

About the putative toxin exposure:

- Do you have any of the suspected poison remaining? Household chemical? Pesticide? Pharmaceutical? Plant? Fungus?
- Do you have the container of the suspected poison?
    - Ingredients? Label information?
    - Did the patient eat the container?
    - Can you estimate the amount the patient ingested?
- Was the suspected poison ingested? topical? liquid? pellets?
- Is the patient or any household member on any medication to which the patient may have access?
- Was the patient given any medications by any person?
- Are rodenticides (quote trade names) being used? Have sick rodents been noticed?
- Are molluscicides (quote trade names) being used?
- Have there been any complaints from neighbours about the animal or its behaviour?

First aid: emergency advice to clients

Physical protection of the patient and the client:

First warn the client about the heightened aggressive tendencies of animals in distress and pain. Advise them on dealing with this if the patient is to be transported or manipulated during first aid procedures, for example, by first applying a muzzle.
If convulsions or excitement occur, advise the client

- to try to protect the patient from injuring itself, and
- not to be concerned that it will "swallow its tongue" (in the interests of client safety).

Begin Decontamination:

Topical exposure:
Additional exposure through ingestion following grooming behaviour is likely.
Advise the client to wear protective clothing including rubber gloves while handling the patient to prevent their exposure to the intoxicant.
Powder intoxicant - attempt removal by using a vacuum cleaner.
Liquid intoxicant - bathe in a mild shampoo or a mild liquid *hand* dishwashing detergent. **Dry and warm the patient after bathing** - hypothermia is a risk of this procedure in animals of small body size (cats, small dogs).

Ocular exposure:
Flush the conjunctival sac **immediately** with unlimited volumes of warm clean water.

Buccal exposure (mouthing toads):
Flush the mouth *from the side* (*not the front*) with running water, for example from a garden hose.

Corrosive Ingestion:
Give milk or water to dilute the substance. **Do not attempt to induce emesis.**

Other Toxin Ingestion within 2-4 hr:
Attempt induction of emesis.
Considerations:

- **Contraindications** to emesis (see below)
- Distance from the veterinary clinic. If the client is within 30 minutes travelling time, it may be better to advise immediate admission and give a reliable emetic under controlled conditions at the clinic. Alternatively, the client could be advised to administer the emetic and then immediately transport the patient to the clinic, taking precautions to deal with vomiting during travel (including collecting the vomitus).

Emetics commonly available in households (see list below for details):

- syrup of ipecac
- hydrogen peroxide
- washing soda crystals
- liquid hand dishwashing detergents
- table salt (note risk of toxicity and inconsistent effectiveness)

Battle orders: other instructions to the client

Bring patients with the following signs to the veterinary clinic **immediately**

- respiratory distress
- neurological abnormalities
- protracted vomiting
- slow or rapid heart rate
- bleeding from body orifices
- weakness
- pale mucous membranes

Bring to the clinic in sealed clear plastic bag or glass containers

- any vomitus
- any package or material that the patient has had access to

- specimens of any plants that have been chewed or partly eaten (with flowers, fruits or both if possible)

Emergency management tasks in descending order of urgency

💣💣 OVERVIEW

The order of urgency should be maintained, but some of these tasks can be executed simultaneously, for example, obtain elements of the history while stabilising vital signs.

① Stabilise vital signs FIRST:
- Airway patency
- Breathing
- Circulation
- Control seizures
- Body temperature

② Obtain the history

③ Evaluate the patient thoroughly
- Sample for clinical pathology tests
- Sample for toxicological assays & other diagnostic tests

④ Decontaminate:
- Block continued absorption of toxin:
  - Physical removal: emetic, gastric lavage, enema, enterogastric lavage
  - Chemical immobilisation: adsorbent ± cathartic, ion exchange resin, precipitating/chelating agents
  - Skin cleansing
  - Eye irrigation

⑤ Administer specific antidote (if available)

⑥ Promote metabolic detoxication & toxin excretion
- Diuresis
- Ion trapping (urine acidification/alkalinisation)

⑦ Provide supportive care
- Maintain renal perfusion
- Gastrointestinal protectants
- Anti-emetics
- Analgesics
- Nutritional support

FURTHER DETAILS

① Stabilise vital signs

There are 4 major goals
- maintain respiration
- maintain cardiovascular function
- control CNS excitation
- control body temperature

Maintain respiration
- Establish a **patent airway**.
- Corrosive substances may cause sufficient damage to the oropharynx for a **tracheostomy** to be needed.

- Immediately provide an **oxygen source** if the patient has any degree of respiratory distress. For immediate short-term administration , use a mask or percutaneous tracheal cannula. For longer-term delivery, use an intranasal cannula, endotracheal intubation or an oxygen cage.
- **Artificial ventilation** may be needed. Monitor ventilation status with arterial blood gas assays, pulse oximetry or both.
- **Doxapram hydrochloride** (Dopram-V® Pharm Tech Pty Ltd) can be given for **respiratory stimulation.** Dosage is IV to effect. The recommended doses of the 20 mg/ml solution for countering anaesthetics are, for dogs & cats: barbiturates - 5.5-11.0 mg (0.28-0.55 ml)/kg; inhalation - 1.1 mg (0.05 ml)/kg, for horses: intravenous anaesthetics - 0.55 mg (0.028 ml)/kg; inhalation - 0.44 mg (0.022 ml)/kg. Dosage can be repeated in 15-20 min if required. Adverse reactions: the dose required to produce convulsions from cerebrocortical stimulation in un anaesthetised animals is 70-75 times the therapeutic dose. Excess dosage can produce hyperventilation and alkalosis.

Maintain cardiovascular function

- Immediately place an **intravenous catheter** to be used to administer therapeutics as required.
- Establish **fluid therapy**: Lactated Ringer's solution is the initial fluid of choice. Make adjustments after assessing serum electrolyte concentrations and blood chemistry results.
- Establish **electrocardiographic monitoring** and correct arrhythmias using standard techniques - any critically ill patient is at risk of arrhythmias and cardiotoxins (e.g. cardiac glycosides, ionophore antibiotics, andromedotoxins) induce life-threatening arrhythmias.
- Have **blood products** available (whole blood, packed red blood cells and frozen plasma). Some toxins produce coagulopathies or haemolysis and these may be needed.

Control CNS excitation

- Animals in status epilepticus are high risk and may need lesser drug dosages for induction.
- Initial control: **diazepam** is the drug of choice
- Diazepam may need to be followed shortly by **muscle relaxants**, for example guaifenesin or methocarbamol
- Long-term control: IV phenobarbitone. Use in parallel with measures to decontaminate and promote excretion of toxins.

Control body temperature

- **Hypothermia** management: Use heating pads, hot water bottles or both as sources of warmth, and "space blankets", bubble-wrap packaging sheets or both for insulation.
- **Hyperthermia** management: Bathe patient in luke warm water until rectal temperature reaches 39.5^{o}C. Sedative or anaesthetic use may rapidly resolve initial hyperthermia through loss of thermoregulatory control, and bathing should not be used.

②Obtain history

Attempt to support a diagnosis of poisoning and to identify the specific toxin and to rule out non-toxic differential diagnoses

- owner's activity
- disruptions to household routine
- access to poisonous substances
- chronology of signs – when was the patient last seen normal, how fast did the illness develop, what was the sequence of sign onset

Provide the client with a history questionnaire to complete (example below: Firth 1995) while patient is being stabilised.

TOXICOLOGICAL HISTORY QUESTIONNAIRE

Date: Time: am/pm

PATIENT INFORMATION
Name of Animal: Age: Breed:
Male or Female? De-sexed? Weight:
Vaccination given within the last year?
Any current medication (including routine medication such as heartworm prevention)?

TODAY'S PROBLEM
What time did you notice anything wrong with your animal?
How long before that had you seen your animal acting normally?
What was the first thing you noticed?

What other signs developed, if any? How soon?

Have the signs become better or worse since you first noticed them? Over what time span?

INFORMATION ON ANY SUSPECTED POISON
Name of the product?
Type of product. Liquid concentrate? Diluted liquid spray? Solid?
Do you still have the container?
How long ago do you think you animal was exposed to the substance?
Where do you think it happened?

YOUR ANIMAL'S RECENT ACTIVITY
Did your animal eat his/her food as usual last night or this morning?
What is he/she normally fed?
Anything different lately?
Has you animal been off your property in the last 24 hours?
Has your animal had any anti-flea or anti-tick products applied in the last 24 hours?

YOUR ANIMAL'S ENVIRONMENT / SURROUNDINGS
Is your animal normally kept inside or outside the house? Or both? Different during day or night?
Is your animal kept in a fenced-in area? Or tied up?
Any access to neighbouring properties (even for a short time)?
Where has your animal been in the last 24 hours?
Has your animal been to rural areas in the last week?

YOUR HOUSEHOLD'S RECENT ACTIVITY
Has there been any gardening done lately?
Any compost, fertilizer or weed killers used within the last week?
Any construction work or renovations underway?
Any mouse/rat baits present in the house/garden/shed/garage?
Any cleaning products used inside or outside the house within the last 48 hours? What?

ANY OTHER COMMENTS OF INFORMATION?

③ Evaluate the patient

Evaluation consists of

- Physical examination
- A clinical pathology database from the in-house clinic laboratory

Physical examination check list for poisoning patients

The list below is based on Bistner & Ford (1995). Adapt this to your particular circumstances by considering (in advance) the signs of common intoxications in your practice area.

EENT (Eyes, Ears, Nose, Throat)
- Mucous membrane colour? Petechiae?
- Pupil size? Normal ocular exam?
- Sensitivity to sound?
- Nose - moist, dry, bubbling, caked with dirt?
- Throat
- Odours recognised on breath?
- Foreign material traces between teeth/on tongue?

Cardiovascular
- Capillary refill time?
- Heart rate?
- Heart rhythm (± ECG)?
- Femoral pulse strength?
- Pulse deficits?

Respiratory
- Rate?
- Character (shallow, laboured, agonal)?
- Auscultation (pulmonary congestion, airway sounds)?

Gastrointestinal/hepatic
- Excess salivation?
- Evidence of vomiting?
- Abdominal palpation - painful?
- Intestinal loops fluid or gas-filled, or ropey?
- Rectal temperature?
- Faecal colour, character, consistency? Sample
- Endoscopy → judge oesophageal/gastric damage from corrosives

Urinary
- Bladder palpable?
- Urine production?
- Urine colour? Sample

Musculoskeletal/neurologic
- Walking or recumbent?
- Weak?
- Ataxic?
- Hypermetric?
- Muscle tremor?
- Increases extensor tone?
- Demeanour?

Skin
- Any wet patches smelling of foreign substances?
- Any erythematous regions?

Peripheral lymph nodes
- Should be normal in most poisonings

Clinical pathology database establishment

- Samples required
  - blood 2-5 ml in EDTA for haematology
  - blood 5-10 ml in heparin for plasma biochemistry

- urine 5-10 ml

- Minimum database from **in-clinic testing**: PCV, total protein, urine SG & dipstick analysis, serum urea & glucose (dipsticks)
- Use data to evaluate dehydration (haemoconcentration), anaemia, azotaemia & source (pre-, renal, post-), hypo- or hyperglycaemia
- Hold excess samples, **collect further samples** or both for further in-clinic tests and for **outside laboratory analysis** as required, such as
    - serum/plasma electrolytes
    - blood gases
    - plasma osmolality
    - plasma chemistry profile (liver and kidney function)
    - complete haemogram (for differential leucocyte count requires 2 thin blood smears made within 20 min of EDTA sample collection)
    - specific toxin assays (if available)
    - plasma or blood cholinesterase

④ Decontaminate: Prevent continued absorption of toxin

Physical removal from GI tract

N.B. Collect vomitus for toxicological assays.

Emetics

Contraindications to emesis:

Species

- **ruminants & horses**
- **rabbits & rodents**

Clinical condition

- **seizuring or comatose animals**
- **neurologically depressed animals**
- **reduced gag reflex**
- **respiratory distress**
- **laryngeal paralysis**
- **bradycardia**

Ingested substance posing a risk of aspiration and/or further upper GI tract damage

- **caustic substances (strong acid, alkali or cationic detergent)**
- **petroleum products (petrol, kerosene, turpentine [paint thinner, white spirit])**

If an emetic doesn't work after 2 doses, try another or commence gastric lavage (Firth 1995).

Emetics generally empty 40-60% of the stomach contents. Best results are obtained within 2-3 hrs of toxin ingestion. Feeding the patient a small moist meal before induction of vomiting can increase the chances of an adequate emesis. [Richardson 2000]

Some drugs have anti-emetic properties and treatment of poisoning by these **may require gastric lavage in the first instance** (Richardson 2000). Examples are phenothiazines, antihistamines, barbiturates, narcotics, antidepressants, *Cannabis sativa*, benzodiazepines and tricyclic antidepressants.

- **Apomorphine**: dogs 0.02-0.04 mg/kg IV, 0.04-0.08 mg/kg IM, conjunctival; cats **not recommended** (extreme excitement induced) (Beasley & Dorman 1990, Murphy 1996, Gibbons 1988, Richardson 2000).
    - Conjunctival route is the most convenient and effects can be titrated to some degree if required by flushing the conjunctival sac after vomiting occurs - mild conjunctivitis consistently occurs after administration (Drobatz 1994).
    - Time to onset: 5 min.
    - Apomorphine is a centrally-acting emetic which stimulates dopaminergic receptors of the chemoreceptor trigger zone (CRTZ) in the medulla oblongata (Hardman *et al.* 1996) and possibly stimulates the emetic centre directly.

- Side effects such as CNS and respiratory depression, ataxia, excitement and protracted vomiting are more common after IV dosage; when severe, these can be reversed with Naloxone @ 0.04 mg/kg IV, SC or IM (Richardson 2000) or metaclopramide @ 0.5 mg/kg IM (Terry King, personal communication 2001). Sometimes undesirable CNS excitation occurs in metaldehyde toxicity (Firth 1995).

- **Syrup of ipecac**: dogs 1-2 ml/kg PO up to a 15 ml maximum total dose, repeated once after 20 minutes; cats 3.3 ml/kg PO (Murphy 1996). 6.6 ml/kg has been used experimentally in cats with minimal side effects (Yeary 1972).
  - Time to onset: 10-30 min. Emesis may take as long as 20 minutes after administration. [Drobatz 1994, Richardson 2000]
  - Cats may find syrup of ipecac objectionable; try diluting it 50:50 with water.
  - Acts by gastric irritation and stimulus of the CRTZ.
  - Repeated doses may be cardiotoxic.
  - Ipecac fluid extract should not be used instead of the syrup, as it is about 14 times more cardiotoxic (Hardman *et al.* 1996). Other side effects can be haemorrhagic diarrhoea and skeletal muscle weakness. Side effects are very rare with use of the syrup formulation.
- **Hydrogen peroxide**: dog or cat 5 ml of 3% solution PO (Murphy 1996); 1-2 ml/kg of 3% solution PO (Drobatz 1994).
  - Time to onset: 10 min.
  - Emesis is induced through mild gastric irritation, is inconsistent and the dose can be repeated once 10 minutes after the initial dose if unsuccessful (Drobatz 1994, Richardson 2000).
- **Xylazine**: dog or cat 0.5-1.0 mg/kg IM (Murphy 1996); dog 1.1 mg/kg IM or SC, cat 0.44 mg/kg IM (Richardson 2000).
  - Time to onset: 5-10 min.
  - Xylazine is an α_2 adrenergic agonist.
  - Side effects outweigh benefits as an emetic in dogs and cats with effects such as bradycardia, hypotension, reduced respiratory rate and CNS depression; these can be reversed with yohimbine @ 0.1 mg/kg IV (Richardson 2000).
- **Washing soda crystals** (sodium carbonate decahydrate): cats - a few crystals PO (Gibbons 1998); dogs - a few crystals PO (Terry King, personal communication 2001)
- **Liquid Dishwashing detergent [for HAND dishwashing, NOT for machine dishwashers NOR laundry detergents]** e.g. Morning Fresh®, Sunlight®, Palmolive®: 1-2 teaspoons PO (Terry King, personal communication 2001). This emetic may not be effective in cats (Beasley & Dorman 1990)
- **Tranexamic acid** (Vasolamin®) in dogs by rapid IV injection @ 25mg/kg; emetic effect is short-lived and patients appear to suffer very little distress after the initial stomach evacuation (Atyeo 2000).
- **Sodium chloride**: **not recommended** because hypernatraemia is possible if emesis fails; dose 1-3 teaspoons + provide water *ad libitum* (Murphy 1996). Time to onset: 5-10 min. This is an inconsistent emetic (Drobatz 1994). Another possible side effect is haematemesis (Firth 1995).
- **Hydergine** (a mixture of dihydroergocornine, dihydroergocristine & dihydroergokryptine; supplied in solution @ 0.3mg/ml): dogs 0.012 mg/kg IV or 0.024 mg/kg SC; vomiting is induced in most dogs within 10 minutes but some dogs are refractory; vomiting is with a minimum of effort and little distress compared to that induced by apomorphine, however apomorphine is preferred because of its more consistent induction of emesis and the shorter latency (Cahill *et al.* 1981).

Gastric lavage

Use only when emesis is ineffective or contraindicated. Emesis is a more efficient method of removal of stomach contents; gastric lavage after emesis has not been shown to retrieve any significant amount of ingesta (Drobatz 1994). If done within 1-2 hr of poison ingestion, gastric lavage can be very effective (Firth 1995). The procedure is messy and may need to be performed outdoors (Firth 1995).

A checklist of equipment required (modified after Firth 1995)

- Large-bore stomach tube with extra fenestrations at one end (for egress from the stomach) 2-3 times the diameter of the endotracheal tube. Special lavage tubes are available which have a wire-cage tip intended to break up ingesta and minimise tube clogging (Evac-Pump, Lyppards Veterinary Supply, Melbourne). Cook gastric lavage tube (Terry King, personal communication 2001).
- Small-bore stomach tube with flared end or funnel attached (for ingress to the stomach)
- Endotracheal tube, cuffed
- Hose-tap connections
- Warm water source
- Obstetrical lubricant
- Mouth gag
- Receptacle for out-flow

The procedure (Firth 1995, Richardson 2000)

- **contraindicated in caustic or petroleum product ingestion**
- use in **unconscious or anaesthetised patients**; isoflurane is optimal, but other anaesthetics may be appropriate (Richardson 2000). Diazepam/ketamine or oxymorphone provide short-duration anaesthesia of the appropriate depth (Firth 1995).
- first place and inflate a cuffed endotracheal tube. This is **mandatory** to prevent aspiration of stomach contents.
- place 2 orogastric tubes: large bore egress tube, small bore ingress tube, in that order
- place tubes to the level of the xiphoid cartilage (premeasure the tubes before passing by lying them alongside the patient from mouth to abdomen, and check their placement by palpation if practical)
- adjust the table so that the patient's head is below the level of its abdomen
- keep one hand on the patient's abdomen to monitor gastric filling. Do not over-distend the stomach.
- flush with at least 5-10 ml/kg fluid (water or saline) at body temperature each time until returning fluid is clear. Avoid too high a water pressure if the ingress tube is joined to a water tap.
- **collect the initial gavage product for toxicological assays**
- it is sometimes helpful to turn the patient from one side to the other (right and left lateral recumbency) during lavage to aid stomach emptying
- at the end of the lavage (returning fluid clear), remove the ingress tube and double check that the endotracheal tube is in place and cuffed.
- leave activated charcoal and a cathartic in the stomach at the end of the procedure
- seal the end of the lavage tube (kink it) before removal to prevent aspiration
- leave the endotracheal tube in place until the patient is semi-conscious to reduce the risk of aspiration

Enterogastric lavage (retrograde)

May be required when potentially-lethal exposures have occurred: strychnine, metaldehyde, tricyclic antidepressants, 5-fluouracil, isoniazid (Richardson 2000).

Complications of this procedure include intestinal rupture and gastroenteritis (Richardson 2000).

- give a pre-anaesthetic dose of atropine (unless contraindicated) to relax alimentary smooth muscle and prevent abdominal distension
- perform a gastric lavage (as above) first, leaving all tubes in place
- perform an enema to remove faecal matter from the colon, leaving the tube in place
- run body temperature water from a tap slowly into the enema tube until fluid exits the gastric lavage tube
- continue until the outflow is clear
- leave activated charcoal in both the stomach and the colon

Enemas

Enemas are useful

- in facilitating the action of cathartics
- where the poison is solid material, such as compost, garbage or pellets (e.g. molluscicide)

A checklist of equipment required (modified after Firth 1995)

- Tubing:
  - Cats - old soft IV tubing or dog urinary catheter (round sharp edges by melting them with a match)
  - Dogs - soft rubber tubing of about 1 cm diameter
- Fluid reservoir:
  - Cats - use an old IV fluid bag
  - Dogs - about 1 L capacity
- Fluid: Premixed enema solutions for humans are contraindicated in dogs and cats because of potential electrolyte or acid-base imbalance - use plain warm water or soapy warm water (Richardson 2000). Activated charcoal may be added (Richardson 2000).

Fluid volume required depends on the size of the patient and the state of its lower intestinal tract. Continue the procedure until the return fluid runs clear.

If there is difficulty with emptying the lower intestine, it is better to repeat the enema in 1-2 hours rather than being too vigorous at the first attempt.

Cathartics

Cathartics are useful for hastening elimination of substances from the alimentary tract, particularly solid intoxicants (for example, compost, garbage, molluscicide pellets). *Non-oily* cathartics can be used in tandem with activated charcoal. Oils reduce the efficacy of adsorption of the activated charcoal.

- **Sodium sulphate** (Glauber's salts): dog and cat 1 g/kg PO (Murphy 1996). 250 mg/kg PO (Richardson 2000). 250-500 mg/kg PO in 10 times the volume of water (Firth 1995).
- **Magnesium sulphate** (Epsom salts): mix dose with 5-10 ml water/kg - dogs 250-500 mg/kg PO, cats 200 mg/kg PO (Gibbons 1998). 250 mg/kg PO (Richardson 2000).
  - Less effective than sodium sulphate (Firth 1995).
  - Contraindicated in CNS depression as hypermagnesaemia will exacerbate the depression, and in patients with compromised renal function.
- **Mineral oil** (paraffin oil): adult horse and cattle 4 litres PO, adult sheep and goat 1 litre PO, adult dog 5-15 ml, adult cat 2-6 ml (Murphy 1996). Not normally absorbed across the alimentary mucosa, but do not use in conjunction with dioctyl sodium sulfosuccinate as emulsification may cause accumulation of indigestible oil in the liver (Firth 1995).
- **Sorbitol**: osmotic cathartic safe to use repeatedly with AC (Richardson 2000). 0.5 g/kg PO (Firth 1995).
- **Bulk cathartics**, e.g. psyllium (Metamucil®) @ 0.5-1.0 teaspoon every 12-24 hr, bran or other vegetable fibre (pumpkin, sweet potato) (Richardson 2000).

Vegetable oil is *not* recommended due to being absorbed across the alimentary mucosa, increasing the absorption of lipid-soluble toxins and theoretically causing pancreatitis (Firth 1995).

Chemical immobilisation

Adsorbents

Adsorbents function by binding chemicals with weak non-ionic bonds at numerous active sites on a complex structure of **very large surface area**. [See boxes below]

Medicinal activated carbon (activated charcoal) is the safest and most effective of the adsorbents listed, but too expensive to use routinely in production animals.

Dry powder adsorbents need to be **mixed into a slurry with water before dosing by stomach tube** (see the individual accounts below for advice on the best methods to use). Either use a face mask or work in a very well-ventilated space when mixing powdered adsorbents (particularly activated carbon) to **prevent inhalation** of the finely-divided material and the minor risk of lung damage (pneumoconiosis).

- **Activated carbon (activated charcoal)**: All species @ 2-8 g/kg PO [1 g AC per 10 ml water] (Murphy 1996). All species @ 1-3 g/kg PO (Richardson 2000), 1-4 g/kg PO (Firth 1995). Ruminants @ 5 or more g/kg.
  - Cathartics should be given to aid the elimination of AC (unless the patient has diarrhoea already) so that the adsorbed toxin is not released in the alimentary tract.
  - Oily cathartics are contraindicated. They interfere with the adsorptive capacity of AC.
  - AC is formulated variously as dry powder, liquid suspensions, granules or compressed tablets. Some formulations contain the cathartic sorbitol. Use the compressed tablets at the higher end of the dose range (they are somewhat less effective than other formulations) - each tablet commonly contains 300 mg AC, so at least 4 tablets are needed per kg body weight.
  - Effective mixing of powdered AC is facilitated by first placing the AC in the mixing container, then thoroughly mixing in a small amount (10-20 ml) of viscous liquid such as Kao-pectate or radiographic barium sulphate before adding water to create a pourable suspension (Frith 1995).
  - Repeated doses of AC every 4-6 hours can be useful in poisoning by toxins with an enterohepatic circulation such as cardiac glycosides.
  - Substances not effectively absorbed by AC include: caustics (alkalis), ethanol, methanol, fertilizers, fluoride, petroleum products, most heavy metals, iodides, nitrate, nitrite, sodium chloride, chlorate (Beasley & Dorman 1990, Richardson 2000).
  - For further information see the box below.
- **Kaolin** (a clay)**, pectin**: 1-2 ml/kg PO q.i.d.- b.i.d. (Gibbons 1998)
- **Bentonite** (a clay mineral): Ruminants 5-10 g/kg PO (McKenzie 1991).
  - Because bentonite is so cheap, it may be feasible to use higher doses. Up to 15 g/kg has been given safely to cattle (PJ Dunster unpublished data cited by McKenzie 1991), but attention must be paid to the degree of ruminal distension caused if this amount is given in a single dose, and dosing stopped if this threatens to interfere with the animal's well-being.
  - Bentonite swells fairly rapidly when mixed with water. Mixing and dosing is facilitated by adding the powered bentonite to a quantity of water while continuously stirring, then adding further water to create a pourable slurry and giving the suspension by stomach tube before it gels.
  - For further information see the box below.

*Activated carbon - the material, its production and uses**

This material is commonly known as activated charcoal in the medical and veterinary professions, probably due to the assumption that the material of origin is usually wood. However, the starting materials for medicinal activated carbons may include peat, coal or other carbonising organic materials. Thus, on the basis of its starting materials, the correct name for this material should be **activated carbon**. However, it should be acknowledged that the material is not pure carbon, but contains inorganic impurities.

Activated carbon has been described as "a very fine, odourless, tasteless, black powder … prepared from vegetable matter … by carbonisation and activation" (Wade 1077). Powdered activated carbons are adsorbents widely used in the purification of solutions in the food, chemical and pharmaceutical industries, in the treatment of municipal water supplies and as therapeutics (Cameron & MacDowell 1972). **Typical medicinal activated carbons have a surface area of the order of 900-1000 m^2/g** (Cameron & MacDowell 1972) and activated carbons as a group have surface areas of 600-1500 m^2/g (Cooney 1980).

The processes used for making activated carbons are **pyrolysis** (**carbonisation**) and **controlled oxidation** (**activation**). The starting materials are organic, and comprise such raw materials as peat, petroleum, coke, coals (bituminous and lignite), sawdust and wood char, paper mill waste (lignin), bone char and coconut shells. These are carbonised under controlled conditions, usually in the absence of air, at 600-900^{o}C. Activation is effected either by chemicals or steam, the two processes producing

end products with different chemical properties. For example, steam activated carbons all contain less than 2% oxygen, while chemically activated carbons may contain as much as 11.4% oxygen.

Chemical activation is done by mixing a chemical (phosphoric acid, zinc chloride) with a carbonaceous material, mostly wood, for carbonisation at a relatively low temperature (about 400-500^{o}C for phosphoric acid), then recovering the chemical for reuse. the chemicals cause the wood to swell, opening up the capillary structure while preventing shrinkage and reducing tar formation to provide a graded conversion of wood to carbon. The pore structure produced is suitable for adsorption without further processing.

Steam activation is a two-stage process beginning with carbonisation of the starting material, producing carbon with pores too small or constricted for effective absorption. This semi-product is reacted with steam at 900-1000^{o}C (sometimes with air or CO_2) to enlarge the pore structure in a controlled manner to various pore-size distributions depending on the intended use of the end product. The time allowed for activation is the most important variable in determining the size of pores and the surface area of the product.

Activated carbon is a **potential fire hazard**. Freshly-prepared carbon may heat spontaneously in air and the presence of water accelerates this. Spontaneous heating and ignition may occur if the carbon is contaminated with drying oils or oxidising agents (Bretherick 1979). the minimal critical temperature for self-ignition of medicinal steam-activated carbon is 92^{o}C (Cameron & MacDowell 1972). Self-heating is related to the oxygen content of the particular activated carbon so that steam-activated carbons that will have been heated to at least 900^{o}C are unreactive and non-hazardous during normal transport. Never-the-less, activated carbons should be stored and handled with their potential for ignition in mind.

Activated carbon is highly effective as an adsorbent of many poisons. It has been experimentally demonstrated to be superior to "universal antidote" (comprising 2 parts activated carbon, 1 part magnesium oxide and 1 part tannic acid) *in vitro* and *in vivo* (Picchioni *et al.* 1966, Cooney 1980). *In vitro* techniques for evaluating its effectiveness against poisons have been developed (Cooney 1980, Kleeman & Bailey 1988). It is valued as an antidote in modern human clinical practice (Cooney 1980, Pond 1986). **As a general rule for use as an antidote, the dose of activated carbon should be about 10 times the weight of the toxin ingested** - in practice , a dose of 100g is recommended for humans, that is, about 1.5 g/kg for the standard 70 kg human. **The type of material to use should be finely powered, relatively free of acid-leachable materials (acid-washed), with a large internal surface area (about 1000 m^2/g) and with a pore size distribution with most pores in the range of 2 nm** (Cooney 1980).

*Activated carbon as therapy for livestock poisoning**

Activated carbon is recommended for all species at 1-3 g/kg body weight, accompanied in most cases by a saline cathartic such as sodium or magnesium sulphate at 1 g/kg (Buck & Bratich 1985, 1986). Different commercial preparations of activated carbon available to veterinarians in the United States had widely different antidotal capacities when tested in rats against carbaryl, strychnine and T-2 toxin. This is a cause for concern and may suggest the need for establishment of official standards of efficiency for commercial formulations of this material. It may also reflect a lack of understanding of the variable nature of activated carbons (which depends on their source material and methods of manufacture) with products being applied to inappropriate uses.

Toxins which are *not* effectively adsorbed by activated carbon include caustic materials, alcohols, fertilizers, fluorides, heavy metals, iodides, nitrate, nitrite, sodium chloride and chlorate (Buck & Bratich 1985, 1986). The simultaneous oral use with activated carbon of mineral or vegetable oils or therapeutic substances of large molecular weight such as antibiotics, vitamins or amino acids is contraindicated. Oils will interfere with the adsorptive capacity of the carbon and the carbon will interfere with the absorption of the drugs (Buck & Bratich 1985, 1986).

In general, it appears that activated carbon is likely to be mainly useful in the therapy of intoxications of livestock when

- the toxin is relatively non-polar (that is, having a relatively low water solubility) if organic, or not strongly dissociated in solution if inorganic

- the carbon is given soon after the ingestion of the toxin
- the rumen acts as a reservoir for unabsorbed toxin
- the toxin undergoes an enterohepatic circulation

A serious disadvantage of activated carbon as an antidote for poisoning of livestock in Australia is its **cost**. The prices from the local importer in Brisbane in late 1988 were $10.88 for a 500 g pack and $247.50 for a 15 kg bag ($16.50/kg). This makes treatment at the presently recommended rates of any but the most valuable livestock a matter for serious consideration by owners and their advisors.

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Bentonite*

Bentonite is a clay mineral composed of smectites of the montmorillonite-beidelite series of aluminosilicates (Grim & Guven 1978). It has a layered (lamellar) crystalline microstructure which allows adsorption of other molecules and account for its marked swelling when added to water. Bentonite has a variety of industrial, engineering, agricultural and miscellaneous uses including the clarification of beverages and water and the decolourisation of oils. Bentonite has been used as an adsorbent with some success in the therapy of experimental paraquat poisoning of laboratory rats (Clark 1971, Smith *et al.* 1974) and cats (Clark 1971), but with little effect in poisoned humans (Park *et al.* 1975). It has been used as a feed additive to prevent growth depression and feed refusal in rats caused by the trichothecene mycotoxin T-2 (Carson & Smith 1983). Hydrated sodium calcium aluminosilicate, a material closely related to bentonite, has been used for preventing aflatoxicosis in growing pigs (Colvin *et al.* 1989, Harvey *et al.* 1989, Beaver *et al.* 1990). Bentonite is cheap, costing about $A0.20/kg. It is more pleasant to handle than activated carbon and is mined and processed in Australia.

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Ion exchange resins

These materials ionically bind certain drugs and toxins.

- **Cholestyramine**: 50-70 mg/kg PO in a slurry with water or other fluid (do not give in the dry state [Firth 1995]).
  - Useful for binding *fat-soluble* toxins such as organochlorine compounds and *acidic* compounds such as digitalis
  - Used to delay or reduce absorption of phenylbutazone, warfarin, chlorothiazide, tetracycline, phenobarbital and thyroid preparations
  - Possible side effects include steatorrhoea, loss of fat-soluble vitamins and constipation
  - Overdose produces hypochloraemic metabolic acidosis

Chelating/precipitating agents

These compounds are used in heavy metal poisoning and in some plant poisonings (alkaloids, oxalates).

- **Sodium thiosulphate** ("hypo"): arsenic, cyanogenic glycosides (ruminants)
- **Sodium bicarbonate** : iron - 1% solution as gastric lavage
- **Magnesium sulphate** : lead
- **Calcium salts** : fluoride
- **Tannic acid** (tea): 1-2% solution (tea); 500-2000 mL as lavage solution
- **Ammonium chloride** : strontium - 200-500 mg PO repeated x 4 at 6-8 hour intervals

Elimination from skin

If the skin or hair coat is contaminated with toxins such as insecticides, petroleum-based products or aromatic oils, removal is indicated

- remember the **heightened aggressive tendencies of animals in distress and pain** and take precautions to avoid personal injury, for example, by applying a muzzle.
- wear rubber gloves and plastic apron to prevent exposure to toxins
- bathe the patient gently and thoroughly with *warm* soapy water, mild hand dishwashing liquid or mild pet shampoo, paying particular attention to areas that the patient may lick (e.g. feet). For petroleum-based products, mechanic's hand cleaner or coconut-oil based soaps are recommended above dishwashing detergent. Work the detergent/soap well into the hair coat with a minimum of water until ready to rinse.
- **dry gently and thoroughly**
- **monitor body temperature after bathing** (hypothermia is a risk in cats and small dogs)
- oil-based paint is best removed by clipping rather than washing with solvents, as solvents themselves are toxic

Elimination from eyes

Eyes may require immediate 20-30 min continuous irrigation with normal saline at body temperature (Firth 1995, Gibbons 1998). Using neutralising agents is not generally recommended. Chemical burns to eyes should be treated with lubricant ointments and possibly temporary tarsorrhaphy. Mydriasis induced with atropine may be useful to try to prevent pupillary adhesions forming. Daily examination to assess progress is mandatory. Topical corticosteroids are contraindicated if the corneal membrane is damaged. Systemic NSAIDs should be used to reduce ocular inflammation.

Poison Decontamination Do's and Don'ts [slightly modified from the ASPCA/NAPCC document]

Do

- Treat the patient not the poison.
- Stabilize the animal before attempting decontamination procedures.

Don't

- Bathe a seizuring animal. (Always stabilize the animal first.)
- Use salt as an emetic agent.
- Use apomorphine as an emetic agent in cats. (This is controversial.)
- Administer xylazine or apomorphine as an emetic in a severely depressed animal.
- Induce emesis in
  - a seizuring, extremely stimulated, or hyperactive animal.
  - a vomiting animal.
  - a severely depressed, lethargic, comatose, or debilitated animal.
  - an animal that has had recent abdominal surgery.
  - an animal that has a megaoesophagus.
  - a bird, rabbit, rat, horse or ruminant.
- Induce vomiting in cases of poisoning by
  - an ingested corrosive agent.
  - hydrocarbon/ petroleum distillate ingestion. (In most cases)
- Administer activated charcoal
  - for most heavy metals, corrosives, or petroleum distillates.
  - to a vomiting animal.
  - to an animal in ileus or a gastric obstruction.
- Administer a cathartic to a dehydrated animal or one with diarrhoea.
- Use a magnesium sulphate cathartic in a renal compromised animal.
- Use pre-mixed enema solutions such as hypertonic phosphate solutions.
- Perform a gastric lavage without using a cuffed endotracheal tube.

⑤ Administer antidotes if available

Note that antidotes or effective specific therapies are **available for only a small proportion of the spectrum of possible intoxications**. See Tables 1-33 to 1-40 (pp.180-210) in Bistner & Ford (1995), Murphy (1996), Firth (2000) and the specific toxin sections of this document.

⑥ Promote clearance or metabolism of absorbed toxin

Promote renal excretion

Toxins that are present in plasma in large amounts, that are ionic and water soluble are most suitable for this approach.

Before commencing these techniques, **IV fluid therapy should be established and adequate** as judged by

- normal central venous pressure - *monitoring this value while pursuing these techniques is strongly recommended to avoid dehydration from diuresis* (Firth 1995).
- mean arterial pressure
- urine output

If any of these values are abnormal, measures must be initiated to ensure adequate renal perfusion, including (but not limited to) constant rate infusion of dopamine

- **Diuresis**: monitor hydration (above) and maintain renal perfusion (see below) -
  - fluids alone
  - mannitol (osmotic diuresis)
  - dextrose (50%) (osmotic diuresis)
  - furosemide.

  Adverse effects of forced diuresis include pulmonary oedema, cerebral oedema, metabolic acidosis or alkalosis and water intoxication (Richardson 2000)
- **Ion trapping**: Ionised substances do not cross renal tubular membranes easily. If urinary pH can be changed so that the toxin is shifted to its ionised form, then it will be trapped in the renal tubule and not resorbed. Acidic compounds such as aspirin are trapped in alkaline urine while alkaline compounds such as amphetamines are trapped in acid urine. Many adverse effects are possible, so this approach must be used judiciously (Richardson 2000). This technique could be useful if
  - the toxin is significantly eliminated in urine unconjugated
  - metabolites have a pKa near the range of common urinary pH
  - the toxin is not highly lipophilic or extensively protein-bound

  Urine acidification
  - **Ammonium chloride** PO: dog 25-50 mg/kg, cat 10 mg/kg, repeated every 6 hours;
  - Contraindication include pre-existing metabolic acidosis, hepatic insufficiency, renal insufficiency, haemoglobinuria or myoglobinuria
  - Monitor serum K andurine pH frequently
  - Ammonia intoxication (*q.v.*) produces depression and coma

  Urine alkalinisation
  - **Sodium bicarbonate** IV: 1-2 mEq/kg repeated every 4 hours
  - Contraindications include pre-existing metabolic alkalosis (particularly a risk with the concurrent use of furosemide), hypocalcaemia, hypokalaemia
  - Monitor serum K andurine pH frequently

Dialysis: peritoneal or haemo-dialysis

Interrupt enterohepatic circulation of toxins

See chemical immobilisation above

Specific enzyme inhibitors

4-methylpyrazole in ethylene glycol poisoning

Specific antibodies

vs. digitalis

⑦ Provide supportive care

Respiratory system support

See above

Cardiovascular system support

See above

Maintain renal perfusion

This is a high priority in the poisoned patient because they are at high risk of renal damage and failure through either direct toxic insult or under-perfusion.

Fluid balance, electrolyte and acid-base control must be accurate and correct.

Establish a protocol to **anticipate and prevent oliguria** and subsequent acute renal failure

Management of patient at risk of acute renal failure (Bistner & Ford 1995, Terry King, personal communication 2001)

- ensure volume loaded (normovolaemic)
- i/v fluid therapy at maintenance rate using balanced electrolyte solution
- urinary catheterisation & collection
- monitor urine output hourly (1-2 ml/kg/hr is the expected minimum)
- monitor central venous pressure every 2 hours
- monitor serum creatinine, urea and electrolytes every 6 hours

Rapid response to drop in urine production to < 1 ml/kg/hr

- initial fluid challenge with colloid - 5 ml/kg Dextrans 70 IV
- if no response within 30 min, give furosemide (cat 1-5 mg/kg; dog 5-12 mg/kg; start with high dose)
- can repeat & increase furosemide dose twice every 15 min
- if no response to furosemide, mannitol 0.5 g/kg IV ONCE ONLY
- if no response to furosemide, commence dopamine constant rate infusion (2-5 mg/kg/min)
- if no response to dopamine infusion, consider peritoneal dialysis *today*

Gastrointestinal protectants

Use with those intoxicants that are irritant or ulcerogenic.

Cimetidine, ranitidine (Ulcerguard® Ranvet), sucralfate and misoprostol may all be useful.

Antemetics (to suppress intractable vomiting)

Metoclopramide (Metonide® Delvet) is commonly used.

Analgesics

These drugs are very appropriate to counter the common effects of poisons such as severe gastroenteritis and burns or ulcerations.

Longer acting narcotic agonist-antagonists are particularly useful, such as butorphanol (Dolorex® Intervet; Torbugesic® Fort Dodge) or buprenorphine .

Nutritional support

Nutritional support (enteral or parenteral) is indicated in patients with gastrointestinal damage or prolonged sedation. Endoscopy may be helpful in assessing the degree of damage from corrosive poisons.

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💣☑ *Investigating Suspected Poisonings in Animals (single & groups): Beyond the immediate emergency*

Investigate methodically

Take History, Examine Animal(s), Examine Environment, Record Findings

- You may reach a satisfactory case conclusion at any point in this process
- A satisfactory conclusion = a diagnosis & an effective management strategy

History taking is *always* important

- Begins a differential diagnosis list
- The history compared with your local knowledge of available intoxicants may lead to an early diagnosis

Clinical examination (be thorough and methodical)

- Refines the differential diagnosis list
- Should include sampling for clinical pathology and toxin assays
- Leads to the start of treatment

Treatment

- The presence of absence of response to specific therapy may aid diagnosis e.g. atropine vs. OP poisoning

Necropsy (be thorough, methodical - include CNS)

- Refines the differential diagnosis list
- Should include comprehensive sampling for toxin assays, histopathology and microbiology

Environment search for likely toxin source

- Should include sampling for toxin assay (feed, water) and confirmation of the source identity (feed, water, plants)
- Prevent further animal access
- Stopping access may aid diagnosis by resulting in no new cases

Record findings in writing - do *not* trust your memory (it *will* fail you)

Collect samples for laboratory examination

- Not required in all cases, but normally useful for confirming a tentative diagnosis and to help refine prognosis
- *Consider the high cost of toxicological assays*. The following data are to give you a feel for the cost of assays.

Toxin(s) or associated analyte	Price per test ($)				
	QDPI*	NSW Agriculture†	WA Agriculture‡	IDEXX-VPS§	VVPS¶
Ammonia (plasma, rumen)			17		
Cholinesterase (serum)	35			32.50	
Cholinesterase (brain)	50				
Organochlorine and/or organophosphate insecticides	60			POA**	
Organophosphate insecticides (chemical residues)		40			
Heavy metal screen (ICP-MS)‡‡	50			85	
Arsenic (qualitative)			20		
Arsenic (tissue, ingesta - quantitative)	80		67		
Lead (blood)	80	33		40	40
Lead (tissue)	80	33	21	85	

Toxin(s) or associated analyte	Price per test ($)				
	QDPI*	NSW Agriculture†	WA Agriculture‡	IDEXX-VPS§	VVPS¶
Cadmium (tissue)			21		
Copper (serum)	20	3.50	10		
Copper (tissue)	80	33	19		
Fluoride (water)	80				
Fluoride (mineral supplement)	120				
Fluoride (bone)	160		70		
Mercury			46		
Iron (serum)			10		
Iron (tissue)			19		
Selenium (tissue)			19		
Zinc (serum)	20		10		
Zinc (tissue)	80	33	19		
Vitamin A	95				
Cyanide, plant (qualitative)	20				
Cyanide, plant (quantitative)	120		108		
Nitrate, plant, aqueous humour (quantitative)	20				
Nitrate-nitrite		11			
Oxalate, plant (quantitative)	60		25		
Strychnine (ingesta, liver, suspected bait)	80		108	85	
Warfarin/coumarins				POA	
Warfarin (ingesta, liver, suspected bait)	100				
Prothrombin time					20
Metaldehyde (ingesta, suspect bait)	80				
Phomopsin			172		
"Complete" poison analysis††				POA	
Algal identification		23.40			
Algal toxin bioassay			104		
Histopathology (routine)		$32.30 per section		basic fee $62 + $10 for each extra tissue up to a maximum of $112	
Histopathology (non-urgent)				basic fee $36 + $10 for each extra tissue (maximum $96)	

* Queensland Department of Primary Industries Veterinary Laboratories 1999-2000; Laboratories at Yeerongpilly (Brisbane), Toowoomba, Oonoonba (Townsville), Rockhampton; Specimens from disease **outbreaks** in **commercial livestock** in Queensland ONLY - No charge; Under other circumstances, submitters may be directed to other laboratories or a

charge may be levied. **N.B. The prices should be taken as guidance only, not firm fees** (data based on Animal & Plant Health Service Fees & Charges effective 30 June 1999)

† NSW Agriculture Regional Veterinary Laboratories; Extracted from Schedule of Fees 1 November 1999

‡ Agriculture Western Australia Animal Health Laboratories, South Perth

§ Veterinary Pathology Services Queensland Laboratory General Price List 1999; Prices generally apply to VPS laboratories in Qld, NSW and SA; Specimens accepted from all species of animals, single and multiple

¶ Victorian Veterinary Pathology Services Routine Test Price List 2000; Extracts from price list of tests relevant to toxicology; Specimens accepted from all species of animals, single and multiple.

‡‡ Heavy metal screen = As, Cd, Co, Cr, Cu, Hg, Mn, Ni, Pb, Se, Zn

** POA = Price on application; expect > $100 per test

†† "Complete" poisons analysis = cyanide, heavy metals, strychnine, metaldehyde, rodenticides, OP & CHC insecticides

Consult your local laboratory for specific advice and *read* their specimen collection guides (if available) e.g. Taylor (2001)

Specimens need to be

- from the **appropriate** tissue or source
- in **sufficient** amounts for the technique requested
- **handled properly**

Handling

- special containers for some assays (e.g. blood for Zn or Cu analysis - ordinary rubber, e.g. in Vacutainer® tops, contains sufficient Zn or Cu to affect the analysis)
- freeze organ specimens for toxicological analysis (if preservation is needed)
- **never** freeze tissue specimens for histopathology (ice crystals disrupt tissues)
- ensure **packaging conforms to regulations** governing transport of dangerous goods (diagnostic specimens) by road and air. A generally-accepted standard is the International Air Transport Authority (IATA) Packaging Instruction 650. Note that failure to do this and subsequent accidental spillage (with or without subsequent contamination of transport workers) could result in criminal prosecution leading to a jail term or serious fine. Conviction of a criminal offence results in removal from the Register of Veterinary Surgeons.

Submission to a veterinary diagnostic laboratory should include

- a **full history** - allows laboratory staff (pathologists and others) to suggest other useful tests or lines of investigation
- a list of **specific tests requested**. N.B. requests for "screening" tests for "any" or "all" toxins are impossible to satisfy. **Be specific**.
- recognition of the limitations of tests and the quality of specimens
- enough specimens to cover the differential diagnoses inherent in a case, including infectious and other non-toxic causes.

Basic appropriate specimens to send to a diagnostic laboratory

It is better to collect too much than not enough. Excess material can always be discarded. It is often impossible to obtain further material after the initial investigation.

Suspected toxin source material *– hand-fed or supplemented animals*

- *Always* collect source material if available because it probably contains the highest toxin concentration and provides the best chance of detection
    - collect about 1 kg feed for confirmatory analyses
    - be aware that **incomplete mixing** often occurs, or that toxin may be **localised** (e.g. in some monensin poisonings of horses, the toxin was all in the bottom of the first bag through the feed mill after mixing a batch of cattle feed).

- in case a feeding trial is needed, collect or have set aside a reasonably large amount
    - if the condition seems related to a single meal of suspect material → estimate of amount needed to reproduce the condition if initial analyses prove negative

Suspected toxin source material *– grazing animals*

- thorough inspection of the pasture, noting plants with evidence of having been grazed or browsed
- collect botanical specimens of suspected plants to confirm their identity
- collect specimens of suspected plants for toxin assays – field spot tests and/or laboratory assays; **do not use plastic bags** for collection or transport of samples because these concentrate moisture around the plant and thus promote microbial breakdown of toxins increasing the likelihood of false negative results
    - suspected cyanogenic glycosides: samples should be presented to a laboratory *unwilted* – dig up root ball, pack root ball in wet newspaper but not the aerial parts of the plant
    - suspected nitrate-nitrite or oxalate: samples may be submitted fresh or air-dried

Stomach contents *(chilled or frozen)*

For toxicological purposes, **stomach contents** include **vomitus and rumen contents** from mammals, and **crop, proventriculus and gizzard contents** of birds. These are not always available as they may have been lost through being vomited (monogastrics) or being passed into the intestines in subacute conditions.

Rumen contents retain many toxins including dense material (e.g. Pb) which gravitates to the bottom of the rumen and reticulum and birds may hold particles of a particular size and density in their gizzards (e.g. lead shot).

However, toxins susceptible to bacterial breakdown (e.g. urea, nitrate, oxalate) need **early** assay or swift special preservation measures to ensure their detection in significant concentrations

Rumen contents may contain recognisable fragments of poisonous plants or their seeds. To investigate rumen samples for these

- collect a representative sample in a 450 ml jar. A few ml of 10% formalin should be added to the sample for preservation. Mix it in well. Do not dry the contents. Report the consistency, smell and water content of the ruminal contents. Look for large, readily-recognisable plant parts, for example, intact leaves, fruits, seeds or flowers, and collect them separately from the rest of the rumen sample. **Note well!** The examination of rumen contents is not a substitute for a collection of suspect plants. The examination of rumen contents is a long, tedious and objectionable task and will usually only be carried out as an adjunct to a field search for poisonous plants by the field investigator and after other evidence of intoxication (such as histopathological lesions) has been obtained. The rumen content will then be examined for the suspect plants that were found in the field search. It is much easier to compare the rumen sample with known plant samples than it is to identify the plant fragments alone and out of context.
- techniques have been developed for microscopic identification of epidermal cells of plants from rumen samples or faecal samples, but these techniques are only offered by specialised laboratories with comprehensive reference material to the local flora prepared in advance (Potter & Ueckert 1997, Bicknell 1990)
- measurement of alkane signatures could be a future method of identifying the presence of particular plant species in rumen contents or faeces. The pattern of concentration of various n-alkanes, one chemical class in the complex chemical mixture comprising plant cuticle wax, is used in studies of plant-animal interactions (Chen *et al.* 2000).

Assay for specific plant (and other) toxins in rumen or stomach contents is an option for some laboratories. Examples from North American laboratories include various alkaloids (*Delphinium, Taxus*) and cardiac glycosides.

Organ samples for toxin assays *(unpreserved or frozen)*

- **Liver**:
    - All blood from the alimentary tract passes through the liver, so incoming toxins are likely to be concentrated in liver, which is also a major excretory organ for toxins
    - 50 - 500g covers most toxin assay procedures [5g = a cube of side 5cm]
- **Kidney**:

- Kidneys are major excretory organs for toxins, so outgoing toxins are likely to be concentrated in kidney tissue
- Collect 1 whole kidney for animals up to sheep size; half an adult ox kidney

Body fluids *(chilled)*

- **Blood**: 10-20ml from live animals
  - for specific tests (e.g. lead, cholinesterase)
  - specific collection conditions may apply depending on requested assay (type of anticoagulant, container, whole blood vs. serum)
    - for **haematology** (complete blood count including differential leucocyte count): 5 ml in EDTA + 2 thin blood smears made within 30 minutes of collection [Note: Do not refrigerate smears as subsequent moisture condensation will lyse cells; EDTA will cause toxic changes to leucocytes after about 30 min, preventing accurate differential leucocyte counts]
    - for **clinical biochemistry** (standard profile): 10 ml clotted blood for serum [Note: Do not refrigerate before clot retraction occurs] or 10 ml in lithium heparin for plasma; for plasma glucose – 5 ml in Fluoride-oxalate anticoagulant
    - for **serology** (antibodies to infectious agents): 10 ml clotted blood for serum [Note: do not refrigerate before clot retraction occurs]
    - for **blood lead** assay: 5-10 ml in EDTA or lithium heparin
- **Urine**: up to 250ml (not often used)
- **Aqueous humour**: Collect as much as possible at necropsy using aseptic technique with a syringe and needle. Place the sample into a sterile bottle and chill it for submission to the laboratory. Bacterial growth in the sample will distort results.
  - nitrate-nitrite confirmation
  - source of clean fluid reasonably representative of serum at time of death
  - apply results cautiously.

Tissues for histopathology *(fixed in 10% formalin, not frozen)*

A suggested range of tissues to collect at each necropsy is:

- Any lesions (5 mm wide slices), plus the following, whether they contain grossly-visible lesions or not
- Heart:
  - Collect 5 mm wide slices from both ventricles, the interventricular septum and both atria. Lesions of heart muscle are often small, focal and scattered. Multiple sections as suggested above provide the best chance of detection.
  - Lesions in heart muscle take some time to become visible histologically after the damage is initiated. Insufficient time may have elapsed for lesions to be visible in animals that die suddenly, despite their heart function being fatally compromised. A rule-of-thumb: for there to be a reasonable probability of lesions being detectable histologically, over 24 hrs needs to elapse between initiation of poisoning and death.
- Lungs
  - Collect 5 mm wide slices from both lungs
  - Lesions in lungs are likely to be non-uniform in distribution – collect affected tissue
- Liver (5 mm wide slices)
- Kidney (5 mm wide slices including cortex and medulla)
- Brain
  - Remove the whole brain intact (cerebral hemispheres, cerebellum and brain stem) and fix it at least overnight in a large volume of formalin before transporting it. Several days fixation is preferred.
  - Do not slice it unless transport conditions demand division into smaller sample sizes. If slicing is required, use a maximum of 2 transverse slices. Try not to slice into the brainstem.

Many cat and dog 'poisonings' turn out to be cardiomyopathies and histopathology of the heart is a vital differential diagnostic tool.

Histopathology acts as both a **diagnostic tool** in its own right and a **quality control standard** against which the results of microbiology, clinical chemistry and other laboratory tests can be compared for relevance and consistency with the syndrome under investigation.

Specimens for microbiology *(swabs in transport medium, aseptically-collected tissues)* for differential diagnoses

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💣☑ Is litigation threatened? *Preparation for a possible court case*

The threat of legal action may be overt or you may consider it likely in circumstances such as

- a feed formulation error in commercial feedstuff leading to heavy stock losses
- death of a valuable animal being fed commercial feed
- a possible claim on an insurance policy relating to the dead animal(s)
- an owner in dispute with neighbours or employees

You need to

- **record facts from clinical and pathological examinations** fully, accurately **in writing** for later preparation of reports for solicitors and for use in court
- **record** in writing the **identity** of the animal(s) being examined from microchip implants, brands, earmarks, ear tags, coat markings, etc. and including sex and age
- **collect** and **label** appropriate **duplicate** specimens for laboratory confirmation of your provisional diagnosis
- **seal** specimen containers (so that any tampering with them will be obvious - signature across joins in the sealing tape)
- maintain **continuity of possession** ("chain of custody") of specimens until they pass to the next responsible agency e.g. police officer, laboratory analyst
- obtain a **receipt** for the specimens from the next responsible agency

The literature on this area of veterinary activity is somewhat sparse. For further reading, see Cornwall (1997) for broad advice on acting as an expert witness as endorsed by the Australian Veterinary Association as well as Baker (1999) for a short article on giving evidence as an expert witness in Australian courts and Rooney & Robertson (1996) on the legal situation with necropsy of horses in North America, particularly for useful discussion of the general approach to acting as a witness in a court case (the specific detail relates to the US legal system only), but *not* specifically for poisoning cases. Furst (1997) provides advice and information based on experience as a toxicologist and expert witness in the United States legal system. Stroud & Adrian (1996) discuss forensic investigation of wildlife mortalities in the North American context including suspected poisonings and expert witness appearances. the general principles they cover apply worldwide.

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☑ *Techniques to manage toxin sources in feedstuffs for handfed livestock (including feedlots)*

Contamination of feed grain in Australia by chemical residues, moulds & mycotoxins and weed seeds has been reviewed by van Barneveld (1999). Broadly, chemical residues of compounds used in grain production and protection (OPs, OCs and synthetic pyrethroids) and toxic weed seeds pose a greater toxic and/or economic threat than mycotoxins under Australian conditions (van Barneveld 1999).

Prevention should always be emphasised to clients.

Options given below

- apply mainly to **phytotoxins and mycotoxins** - specific applications are listed under each technique
- are **limited** in their application
- are aimed at **salvaging** hazardous feed where possible instead of completely discarding it in order to produce a management solution that minimises cost to the client. For detail on mould damage/mycotoxins management in Queensland, see Blaney and Williams (1991*a,b*) and Chapter 4.

Stock Feed Regulations (under various names) are

- intended to prevent the presence of harmful substances in commercial livestock feed
- administered by state government agencies
- **fallible** in their aim from time to time and field veterinarians should be prepared to deal with the consequences to their clients.

Assay of feed grain for toxic contaminants

Existing and potential methods for assay of feed grains for some common intrinsic toxins are reviewed by Petterson *et al.* (1999) [minerals, amino acids, tannins, protease inhibitors, saponins, lectins, quinolizidine (lupin) alkaloids, pyrimidine glycones (vicine, convicine), glucosinolates] and Wrigley (1999) [mycotoxins, pesticides]. Newer methods include immunoassays (e.g. enzyme-linked immunosorbent assay – ELISA) for such toxins as alkaloids, glucosinolates, phytoestrogens, mycotoxins and pesticides and have wide potential application to other toxins (Wrigley 1999). Rapid immunoassays have been developed to detect many pesticides in grain including organophosphorus compounds, organochlorines, carbamates, pyrethroids (Gee *et al.* 1995).
Note that these methods, while developed and reported in the literature, may not be available at local laboratories or even within Australia as a whole.

Techniques available to salvage contaminated or intrinsically toxic feed include:

- **Separate the toxin source and discard**
- **Dilute with non-toxic feed**
- **Add non-specific adsorbents**
- **Add or administer specific detoxicating/binding agents**
- **Heat deactivate**
- **Crush/grind and expose to sunlight**
- **Ensile fodder crops**
- **Feed to less-susceptible livestock**
- **Promote existing detoxication mechanisms**
- **Immunise against specific toxins**
- **Manipulate the rumen flora**

Separate the toxin source and discard

- *Toxic weed seeds & ergot sclerotia*: Various techniques are available through seed graders, including screening (differentiate by size) and flotation (differentiate by density). Automated image analysis systems have potential for detection and removal of contaminants of feed grains such as weed seeds and ergots (Wrigley 1999).

Dilute with non-toxic feed

- *Toxic weed seeds, mycotoxin-contaminated grain, toxic hay*: When separation and discard is either not practical or not desired by the client and a source of uncontaminated feed is available with the means to thoroughly mix the two batches. The final mixture should be assessed to ensure that the toxin concentration has been reduced to acceptable values.

Add non-specific adsorbents

- *Mycotoxin-contaminated grain*: Increase the bentonite content of feedlot rations from the normal 2% to 4%. Other clay minerals have been used, for example zeolite, aluminosilicates. This option will not be uniformly successful (Williams *et al.* 1994)
- *Cyanobacteria (cyanophytes, blue-green algae)*: Activated charcoal filtration systems may be used to remove toxins from water supplies, but these are an expensive option.

Add or administer specific detoxicating/binding agents

- *Cotton seed (gossypol)*: Ensure that an adequate intake of calcium is maintained
- *Nitrate-containing fodder & hay*: Experimentally, sodium tungstate (wolfram) has been used to prevent nitrate-nitrite poisoning in cattle with daily doses of up to 6.6 mg/kg *per os*
- *Aflatoxin-contaminated feedstuffs*: The combination of ammonia (0.6-4.0%), heat and moisture (10-20%) can be effective in reducing the aflatoxin concentration in feeds (e.g. cotton seed, maize) without producing adverse effects on cattle subsequently fed the material.
- *Mycotoxin (aflatoxin, patulin, cyclopiazonic acid, ochratoxin, secalonic acid D, zearalenone)-contaminated feedstuffs*: Ozone gas in high concentration is effective for oxidation of certain mycotoxins in feeds e.g. grain (McKenzie *et al.* 1997)

Heat deactivate

- Pelleting may reduce the toxicity of some compounds, for example ricin from *Ricinus communis* (castor oil plant).

Crush/grind and expose to sunlight

- *Argemone* spp seed alkaloid concentrations are reduced to non-toxic amounts if the seeds are crushed/ground and exposed to sunlight for 25-30 days. Concentrations were halved after about 15 days.

Ensile fodder crops

- *Cyanogenic glycosides*: Forage sorghum containing hazardous concentrations of cyanogenic glycosides may be rendered non-toxic by ensiling. The cyanogenic potential of the silage should be checked before feeding. *Note well*: Hay from hazardous forage sorghum retains its cyanogenic potential.
- Ergot alkaloids and other alkaloids will apparently survive the ensiling process.

Feed to less-susceptible livestock

- *Pyrrolizidine alkaloids*: It may be possible to salvage pyrrolizidine alkaloid-containing feed by feeding it to sheep or goats if other options are not available or not practical.
- *Deoxynivalenol (vomitoxin)*: → ruminants, poultry, horses
- *Fumonisins* → ruminants

Promote existing detoxication mechanisms

- *Nitrate-nitrite*: Increasing the carbohydrate intake of cattle, for example increased grain or molasses in the diet, will increase the capacity of the ruminal flora to metabolise nitrate through nitrite to ammonia.

Immunise against specific toxins

- *Phomopsin*: Work on the production of a commercial immunogen to prevent lupinosis is well advanced, with successful field trials completed.

- Candidate toxins for commercial immunogen development must meet several criteria that ultimately limit this approach to a very small number of phytotoxins and mycotoxins (McKenzie 1994, Edgar 1994). McKenzie (1994) defined the properties of a reasonable prospect for research and development of an immunogen against plant-associated toxins to include
  - being a syndrome that causes little initial tissue damage and is of slow onset
  - being a widespread syndrome of frequent occurrence, relatively large economic significance and preferably with an international distribution
  - having a potentially large, steady and cheap supply of toxin or its source plant
  - having a toxin that is readily degraded by the body's detoxification mechanisms after capture by antibodies

Manipulate the rumen flora

- See Weimer (1998) for an overview.
- *Nitrate-nitrite:* A *Propionobacterium* has been developed and released commercially in North America to aid the ruminal flora in the detoxication of nitrate. It is intended that the organism be inoculated before access to feed with hazardous nitrate concentrations.
- *Mimosine:* Inoculate cattle with mimosine-degrading bacteria before exposure to fodder from *Leucaena leucocephala* shrubs.
- *Fluoroacetate*: a genetically-manipulated bacterium has been developed to detoxify fluoroacetate in the rumen. It has not been commercially released because of concerns about potential for transfer of the organism to feral animals (goats, rabbits) leading to difficulties with their control and subsequent adverse environmental impacts.
- *Pyrrolizidine alkaloids*: Inoculation of cattle with rumen fluid from sheep could be protective (Johnston *et al.* 1998).
- Candidate toxins that may yield to research using this approach include
  - *Pimelea* spp. toxins (St.George disease) through genetically-modified bacteria
  - hydrolysable tannins through flora transfer from sheep to cattle
  - nitrotoxins
  - lantadenes
  - steroidal saponins

Practical issues that impinge on the effectiveness of ruminal flora manipulation for prevention of intoxication include

- identification of candidate bacteria with
  - the required detoxication capacity and that can themselves persist in the rumen in useful numbers. Potential sources: ruminal floras of animals (the same or different species) resistant to the candidate toxin.
  - genes coding for detoxifying enzymes that can be engineered into ruminal bacteria. Potential sources: microbial floras of plants containing the candidate toxin or soils in which these plants grow.
- biosecurity concerns arising from the use of genetically-modified organisms
- establishment of such bacteria in the rumen of susceptible animals
- achieving ruminal populations of detoxifying bacteria sufficiently large to counter influxes of toxin effectively. This technique is more suited to countering subacute or chronic toxicity and runs the risk of being overwhelmed by sudden large influxes of toxin such as occur in acute poisonings.
- persistence for useful periods of time in the rumen of susceptible animals under field conditions. Seasonal fluctuations in the inflow of toxin to the rumen may be so great that the detoxifying bacteria may die out for want of suitable substrate.
- production of commercial quantities of the detoxifying bacteria
- effective delivery of the bacteria to animals in need of protection. Anaerobic bacteria adapted to life in the rumen require special transport conditions.

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