Permethrin poisoning

Permethrin is one of the most common poisons affecting cats. In most cases they are exposed to concentrated canine spot-on flea treatment products, either through accidental application or secondary contamination from a treated dog. Permethrin poisoning typically causes body tremors and twitching, hyperaesthesia, seizures, pyrexia, ataxia and dilated pupils which can take hours or days to manifest. Treatment usually involves prolonged hospitalisation and is aimed at controlling tremors and seizure activity, dermal decontamination, maintaining body temperature and good nursing care. Recently lipid infusion has been shown to be a very promising treatment in the management of permethrin toxicosis in cats.

Permethrin is a synthetic pyrethroid. Pyrethrins are naturally occurring insecticides extracted from the flowers of Chrysanthemum cinerariasefolium. Pyrethrins and pyrethroids are insecticides used therapeutically on animals (cats, dogs, rodents, birds, cattle, poultry, horses, goats and humans), and to prevent/treat domestic and agricultural insect infestations. Preparations are available for home and agricultural use as dusting powders, liquids, bait stations (usually a small plastic receptacle which contains a small quantity of insecticide and an attractant such as peanut butter), and sprays, or to be used directly on animals as spot-on treatments, shampoo, flea sprays or flea collars.

Exposure in cats
Cats are typically poisoned with permethrin when they come into contact with a canine spot-on flea treatment. This usually occurs after the product is applied to the cat in error or after the cat comes into contact with a treated dog. There are a few products licensed for use in cats (mostly flea collars and flea powders). The flea powders contain a low concentration of permethrin (1% or less) and do not seem to cause the signs seen with canine spot-on products which in contrast contain much higher concentrations.

Key point
Cats are typically exposed to permethrin when dog flea products are applied in error, or they come into contact with a treated dog.
of permethrin (e.g., some spot-on products contain 744 mg/ml, so is 74.4% permethrin). Toxicity has also been reported with spot-on products that contain 45–65% permethrin. Individual response in cats is variable and toxicity can occur from a drop of a highly concentration canine spot on product.2

**Mechanisms of toxicity**
Pyrethroids and pyrethrins cause hyperexcitability in cells by slowing the opening and closing of sodium channels in nerve membranes. Signs of poisoning are therefore neuroexcitatory in nature.

In most mammals pyrethrins and pyrethroids are rapidly biotransformed and detoxified by ester hydrolysis or oxidation and as a result these compounds are of relatively low toxicity. The feline liver, however, is relatively inefficient at glucuronide conjugation. This leads to slow excretion and accumulation of metabolites and may be the reason for the increased susceptibility of cats to permethrin poisoning. Pyrethroids and pyrethrins are lipophilic and if repeatedly administered can accumulate in fatty tissues.

A number of studies,3–6 have noted that toxicity is more common in young cats (<4 years, particularly <1 year) but the reason for this is unclear. It may be due to small samples size in studies.

**Clinical signs**
Clinical signs may occur within a few hours but can take 24–72 h to manifest.5 Typically there is body tremor and twitching, hyperaesthesia, seizures, pyrexia, ataxia and dilated pupils. Less common effects include ear flicking, head tilt, hallucinations, dyspnoea, cyanosis, temporary blindness and cardiac arrhythmias. Potential complications include pyrexia or hypothermia, aspiration pneumonia, apnoea, respiratory or cardiac arrest.6 Prolonged controlled seizure may result in cerebral oedema, irreversible brain damage

<table>
<thead>
<tr>
<th>Source</th>
<th>Deaths/total cases</th>
<th>Fatality rate</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>1/20</td>
<td>5%</td>
<td>Dymond and Swift 20084</td>
</tr>
<tr>
<td>Sweden</td>
<td>7/77</td>
<td>9%</td>
<td>Holmgren and Hulten 200719</td>
</tr>
<tr>
<td>VPIS data</td>
<td>30/286</td>
<td>10.5%</td>
<td>Sutton et al 20078</td>
</tr>
<tr>
<td>Australian Pesticides and Veterinary Medicines Authority’s Adverse Experience Reporting Program</td>
<td>6/26</td>
<td>23%</td>
<td>Linnett 20085</td>
</tr>
<tr>
<td>A single veterinary hospital, Australia</td>
<td>8/42</td>
<td>19%</td>
<td>Boland and Angles 20106</td>
</tr>
<tr>
<td>UK Veterinary Medicines Directorate (VMD)</td>
<td>10/27</td>
<td>37%</td>
<td>Gray 200020</td>
</tr>
<tr>
<td>US Environmental Protection Agency (EPA) incident data</td>
<td>39/87</td>
<td>45%</td>
<td>Meyer 19991</td>
</tr>
<tr>
<td>Survey of Australian veterinary practitioners</td>
<td>166/750</td>
<td>22%</td>
<td>Malik et al 20109</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>267/1315</strong></td>
<td><strong>20%</strong></td>
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</tbody>
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and breakdown of muscle tissue could cause myoglobinuria-induced nephropathy. 7

In a review of 286 cases the mean overall recovery was 61.5 h (range 3 h to 7 days). 8 In a review of 41 cases the mean hospitalisation time was 3 days (range 0.5–11 days). 6

**Prognosis**

Prognosis depends on the severity of signs. Various studies have determined the fatality rate in cats poisoned with permethrin to vary from 5–45% (Table 1). Treatment may be required for several days and in some cases cats are euthanased because of cost issues. In one study, 5.2% of cats were euthanased due to financial constraints. 9 In addition, these studies do not include cases where lipid infusion was used. It is possible that treatment with lipid infusion may have reduced the fatality rate in permethrin toxicosis in cats. The prognosis is poor in cats with uncontrolled seizure activity.

**Tip**

Cats should be washed with lukewarm water and washing up detergent to remove the permethrin from the skin.

**Diagnosis**

There are no routine tests to confirm permethrin exposure. Diagnosis is usually based on clinical signs and history of the use of a spot-on flea treatment. Cats treated with a spot-on product may have a greasy patch on the back of the neck. Differential diagnosis will include metabolic abnormalities (eg, hypocalcaemia, hypoglycaemia), intracranial disease, trauma and other toxicities (eg, metaldehyde, strychnine, tremorgenic mycotoxins, lead poisoning, bromethalin).

**Treatment**

**Decontamination**

Cats with tremors or seizures should be stabilised before decontamination, as handling can exacerbate tremors or seizure activity.

**Ingestion**

After ingestion permethrin is rapidly absorbed and so emetics are unlikely to be of use. In addition unless there is significant oral exposure oral decontamination is generally unnecessary. The effectiveness of adsorbents is questionable due to the non-polar nature of these agents (activated charcoal does not bind well to non-polar molecules) and is best avoided because of the risk of seizures.

**Dermal**

Cats should be washed with lukewarm water and detergent (pyrethrins and pyrethroids are not water soluble). The use of hot water should be avoided as this increases dermal perfusion and may result in increased dermal absorption. Cats with long hair may need to have exposed areas clipped. Care should be taken to dry the animal well. A decrease in body temperature may exacerbate effects due to an inverse relationship between sodium influx and temperature. 3 Following decontamination the cat should be collared to prevent grooming and also isolated from other animals to prevent cross contamination.

**Management of increased muscular activity**

Diazepam may be of use to control increased muscular activity (twitching, fasciculation or convulsions) but severe neuromuscular activity may be difficult to control with diazepam alone. Methocarbamol, a centrally acting skeletal muscle relaxant, has been effective where
Keeping cats safe

benzodiazepines have failed. Methocarbamol, however, has limited veterinary availability and experience in the UK. In addition it is only available as tablets however, these can be crushed and given either via a gastric tube in sedated animals or rectally. A combination of diazepam and methocarbamol can be used for refractory convulsions. Barbiturates of full anaesthesia with propofol may be required in severe cases.

Lipid infusion

Lipid infusion is a relatively new treatment which can be very effective in the management of poisoning with lipophilic compounds such as permethrin. It uses the intravenous administration of lipid emulsion (see Box 1) which is more commonly used as parenteral nutrition cases.

The exact mechanism of action of lipid infusion is not fully understood but various hypotheses have been proposed. The lipid component formed in the blood may act as a ‘sink’ or ‘shuttle’ leading to redistribution of the toxic compound.

Lipid infusion has been used successfully in cases of permethrin poisoning in cats. A randomised, controlled clinical trial in cats with permethrin toxicity compared cats treated with and without lipid infusion. The study used a specially designed and validated system describing six clinical stages of poisoning. The study found that cats treated with lipid infusion improved earlier than cats that did not receive the infusion.

Administration of lipids in animals receiving therapy with lipophilic drugs such as propofol has been raised as a potential concern; however the use of lipid is expected to reduce the need for such emergency therapy. The potential effect of lipid infusion on concentrations of other therapeutic agents, including antidotes, should be assessed on an individual case basis. Only a small quantity of lipid crosses the blood brain barrier and for propofol at least the effect of lipid on propofol-induced sedation is expected to be low.

Early use of lipid infusion is recommended if the exposure is thought to be significant, the cat has significant neurological signs or is failing to respond to other therapies. Rapid improvement can occur in cats with permethrin poisoning given intravenous lipids.

Other care

Good nursing care is essential as cats may require sedation for a prolonged period. Body temperature should be monitored closely because it can fluctuate due to tremors, bathing and the use of sedatives or muscle relaxants. Intravenous fluids may be helpful to

Box 1: Lipid infusion regimen

There is no standard regimen for lipid infusion in the management of poisoning.

- Usually, 1.5 ml/kg of a 20% lipid emulsion is given intravenously as a bolus dose. A bolus dose of up to 4 ml/kg in dogs is also suggested.
- This is followed by an infusion (0.25 ml/kg/min over 30–60 minutes). This can be repeated once or twice and if no response can be discontinued. If there is a response it is generally repeated when signs recur.
- Intermittent bolus doses of 1.5 ml/kg every 4–6 h for the initial 24 h has also been used.

The most commonly used product is Intralipid 20% but other products are available.

icatcare.org/felinefocus
Lipid infusion is a very promising treatment for permethrin toxicosis in cats. Aggressive treatment with control of seizures is necessary in severely affected cats. Airway protection may be required in some cases depending on the degree of sedation necessary to control seizure activity. Cooling measures should be used carefully, as a low body temperature may lead to increased toxicity. Atropine is not an antidote to permethrin toxicity and may exacerbate tachycardia which is often present in cats with permethrin toxicity.

Prevention
It is important to educate owners on the risks of permethrin to cats and in households with both a dog and cat to provide information on flea treatments that are safe for both species (see Figure 1).

Figure 1: International Cat Care’s permethrin campaign poster. (Download at: http://icatcare.org/sites/default/files/PDF/permethrin_poster_vet.pdf)

Conclusions
Permethrin is one of the most common poisons affecting cats. It causes severe neurological signs necessitating prolonged treatment and hospitalisation. Cats can survive if treatment is prompt and aggressive with control of seizures. Lipid infusion is a very promising treatment in the management of permethrin toxicosis in cats.

References