

PERMETHRIN INTOXICATION OF CATS

BIBLIOGRAPHY

SUMMARY

A search of the literature using Pubmed and CAB combined with searches of the reference lists of each retrieved article identified 92 publicly available descriptions of pyrethroid use in cats. Intoxication of cats exposed to pyrethroids, principally permethrin (but also fenvalerate, phenothrin, deltamethrin and etofenprox), was reported by authors from 12 countries (Australia, Canada, France, Germany, Italy, New Zealand, Norway, Spain, Sweden, Switzerland, United Kingdom and the United States of America). Evidence in support of the peculiar sensitivity of cats to pyrethroids seems to have been first noted by Beasley and Trammel (1989) and Trammel and Buck (1990), reinforced by Hansen et al (1994) but not widely appreciated until the reports by Volmer et al (1998) and Meyer (1999) who highlighted the significant toxicity to cats of high concentration permethrin spot-on products intended only for topical use in dogs. It is now very clear that cats are much more sensitive to permethrin than dogs. However, the reason for the increased sensitivity of cats is not known (though pharmacogenomic analysis of pyrethroid sensitive sodium channels may be enlightening) and the minimum toxic dose to cats (by any route of exposure) is also not known. Intoxication of cats is now almost invariably associated with inappropriate use of topical permethrin products labelled only for use in dogs. Cats are intoxicated by primary (intentional or accidental) direct application or by secondary exposure to treated dogs. The time after treatment at which dogs no longer represent a hazard to cats is not described. Meyer (1999) reported intoxication of a cat in contact with a dog 48 hours after treatment. Despite label changes in the USA, UK, France and Australia reports of permethrin intoxication in cats continue to be made. Renewed and creative efforts are necessary to effectively mitigate a preventable cause of serious morbidity and mortality in cats.

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
(2000). "AVMA comments on permethrin toxicosis." <u>Journal of the American Veterinary Medical Association</u> 216 (11): 1702.	2000	USA	Adverse reactions by cats to concentrated spot-on, flea-and-tick products that contain permethrin prompted the AVMA Council on Biologic and Therapeutic Agents to make a recommendation to the AVMA Executive Board suggesting product labelling for safety. The US Pharmacopoeia Veterinary Practitioners' Reporting Program coordinator is also seeking comments from the AAHA, AAFP and American Board of Veterinary Toxicologists on toxicoses involving cats exposed to permethrin. The board approved a position statement on inappropriate exposure of cats to concentrated permethrin products and send a letter to the EPA. The letter says that unintended species-specific toxicoses can be prevented. It suggests that product labelling include prominent warnings about exposure of cats to permethrin, the product's toxic and potentially fatal effect on cats, toxicoses in cats, a suggestion to contact a veterinarian in the event of signs of toxicosis in cats, and indication that cats in close contact with treated dogs might develop signs of toxicosis. The July 15, 1999 JAVMA feature "USP – Reporting Back to You" [Meyer 1999] addressed toxicosis in cats following use of concentrated permethrin products.
(2000). "Toxicosis in cats erroneously treated with 45 to 65% permethrin products (vol 215, pg 198, 1999)." <u>Journal of the American Veterinary Medical</u>	2000	USA	

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<p>Association 216(5): 729-729. (2007). "Cats 'killed by flea treatment'." Saturday, 10 November 2007, 10:35 GMT. Retrieved 10 March, 2009, from http://news.bbc.co.uk/1/low/uk/7088397.stm.</p>	2007	UK	<p>Hundreds of cats may have died because their owners mistakenly treated them with anti-flea products intended for dogs, a study suggests. The Veterinary Poisons Information Service found that one in 10 cats referred to it had died after being exposed to permethrin. The chemical is used in flea treatments for dogs but is very toxic to cats, said Alex Campbell of VPIS. VPIS wants clearer warnings to be displayed on canine treatments. Mr Campbell said the substance was present in many products, but in very low concentrations. If accidentally applied to cats they can show "severe clinical signs" and need two or three days of intensive veterinary treatment if they are to survive. Convulsions "You'd find it in ant powders and a few things like that, but in those sort of products it's in very low concentrations, so it doesn't usually cause problems in either cats or dogs," he told BBC Radio 5Live. "However, it is occasionally used in spot-on flea treatments for dogs and if you accidentally apply these to cats, or you've treated your dog and your cat comes into contact with the dog, and actually manages to groom some of it off or whatever, then potentially the cat can get severe clinical signs. "This substance is very toxic to cats." In a study of 286 cases in which canine spot-on permethrin preparations had been used on cats found that 97% showed signs of poisoning. Around 90% displayed symptoms of twitching and convulsions, with one in 10 dying or having to be put down. However, Mr Campbell said poisoning may be more widespread as not all vets report every case, nor do they all use the VPIS, which is part of Guy's and St Thomas' NHS Foundation Trust.</p>
<p>(2007). "Pink page 2: Permethrin." <u>Journal of Feline Medicine & Surgery</u> 9(5): VI-VI.</p>	2007	UK	<p>Refers to: Clinical effects and outcome of feline permethrin spot-on poisonings reported to the Veterinary Poisons Information Service (VPIS) London, Sutton NM, Bates N and Campbell A(2007) <i>Journal of Feline Medicine and Surgery</i> 9, 335 highlighted the lethal risks of permethrin-based dog spot-on treatments being inappropriately applied to cats. A joint press release by VPIS and the Feline Advisory Bureau drew attention to the problem. The report is a review of 286 cases reported to VPIS where such canine spoton permethrin preparations have been used on cats. Of these cases, 97 per cent of the cats had signs of poisoning, 88 per cent had twitching or convulsions and 10.5 per cent of the cats died or were euthanased. Although these data are startling, the VPIS feels that they are an under-representation of the scale of the problem. The veterinary press often receives letters on the topic from vets in practice and the Veterinary Medicines Directorate (VMD) highlighted the problem in 2000 – 'These spot-on products are sold through UK pet stores or supermarkets and veterinary surgeons should be alert to the possibility of being presented with feline cases' (Gray, <i>Veterinary Record</i> 147, p556). Permethrin is one of a group of insecticidal compounds called pyrethroids, which have widespread use in pet flea treatments, ant-killers, and other products for control of pest insects. Although pyrethroids are considered to have</p>

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			<p>a low mammalian toxicity, they are toxic to cats because of metabolic deficiencies found only in felines. In the main problems seem to occur when they have been mistakenly or unwittingly used on cats, frequently causing severe illness and even death. Cats poisoned with permethrin may need two to three days of intensive veterinary treatment (see the veterinary section of the FAB website www.fabvets.org for an article on treatment). There is more information on the different flea products available in the UK and how they work on the FAB website http://www.fabcats.org/owners/fleas). Does this problem occur in other countries? Let us know via claire@fabcats.org</p>
<p>(2007). "VMD advice on permethrin." <u>Veterinary Record</u>. 161(24): 801-.</p>	2007	UK	<p>The Veterinary Medicines Directorate (VMD) has issued a warning to members of the public about the dangers of using permethrin spot-on products on cats. In a notice on its website (www.vmd.gov.uk), the VMD lists 21 products containing permethrin that are intended for the treatment of fleas and ticks in dogs only. 'Some pet owners apply spot-on products containing permethrin that are indicated for use in dogs to their cats by mistake, or because they think that it is safe if they use only small amounts of the product,' it says. However, it warns, 'It is not safe to use any spot-on product containing permethrin in cats.' The VMD advises any owner who has applied any of the products listed to their cat to wash the product off using water and a mild detergent and to seek immediate veterinary treatment.</p>
<p>Anadón, A., M. R. Martínez-Larrañaga, et al. (2009). "Use and abuse of pyrethrins and synthetic pyrethroids in veterinary medicine." <u>The Veterinary Journal</u> 182(1): 7-20.</p>	2009	Spain	<p>Cats are more likely than dogs to developed pyrethroid toxicosis as the feline liver is inefficient at glucuronide conjugation. But there are other reasons too, although the explanation why cats are so sensitive to permethrin has still not been fully elucidated (Gfeller and Messonnier, 2004). The low concentration compounds approved for cats contain 0.05–0.1% of permethrin and do not seem to cause the signs that the concentrated (45–65% permethrin) canine spot-on products do (MacDonald, 1995). Most brands of permethrin 'spot-on' products are labelled for 'use in dogs only' and may be obtained over-the-counter. Permethrin toxicity usually occurs when the owner applies the dog spot-on product but cats that actively groom or engage in close physical contact with recently treated dogs may also be at risk of toxic exposure. The severity of permethrin toxicity varies with each individual animal. Some cats develop signs with only 'one drop' while others show no clinical signs after an entire vial has been applied. Overall, overdosing small pets is easier than overdosing large pets due to the larger body surface- to-weight ratio (Gfeller and Messonnier, 2004). The onset of clinical signs is usually within a few minutes up to hours after exposure, but may be delayed up to 24 h (i.e. as a result of prolonged exposure from dermal absorption or grooming), and in some cases effects can last for 3 or more days. The most common clinical signs of permethrin toxicity in cats are muscle tremors and seizures. Hypersalivation, depression, vomiting, anorexia and even death may also be seen. In a</p>

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			retrospective study of 87 cases of pyrethrin and pyrethroid intoxication in cats, central neuropathies were reported to be the most common clinical signs (Whittem, 1995). These manifest primarily as hyperexcitability, tremors, or convulsions and have been reported to occur in 69% of intoxicated cats. Skeletal muscular weakness and fasciculations, which are signs of peripheral neuropathies, occurred in 28% of affected animals. Clinical signs were evident only in cats <4 years of age, with more than half the intoxicated cats <12 months. From 1992 to 2000, the London Centre of the Veterinary Poisons Information Service (VPIS) received about 50 inquiries per annum regarding pyrethroids and pyrethrins in animals. Permethrin toxicosis in dogs is much less common than in cats. Since January 1999, VPIS recorded 98 feline and 17 canine permethrin cases. The clinical signs (including number of cases) observed in these toxicity cases were as follows: (a) Cats: convulsions (33), muscle fasciculation/ tremor (24), twitching (22), salivation/frothing/ foaming (21), mydriasis (18), hyperaesthesia (7), ataxia/ incoordination (14), shaking/shivering (10), pyrexia/hyperthermia (10); (b) Dogs: convulsions (3), salivation/frothing/ foaming (1), ataxia/incoordination (1), shaking/shivering (1), pyrexia/hyperthermia (2) (Martin and Campbell, 2000).
Australian Veterinary Association. (2008). "Cat owners accidentally poisoning their pets. ." Retrieved 24 August, 2009, from http://avacms.eseries.hengsystems.com.au/AM/Template.cfm?Section=Home&CONTENTFILEID=3150&TEMPLATE=/CM/ContentDisplay.cfm .	2008	Australia	19 November 2008. Cat owners accidentally poisoning their pets. With summer coming, vets are worried about the number of cats they are seeing that have been accidentally poisoned by common flea treatments available in supermarkets. The Australian Veterinary Association (AVA) is telling cat owners to take extra care when buying flea treatments for their moggy as the weather warms up. "Some spot-on flea products for dogs available at supermarkets contain a chemical called permethrin," said Dr Mark Lawrie, President of the AVA. "The treatment is safe for dogs but it's really dangerous when used on cats. People poison their cat by accident - buying a flea treatment they think will cost less and not reading the label properly. "Our members have started to notice that there are more poisoning cases than previously thought. Some preliminary research is backing this up, and more investigation is underway. "When a cat is poisoned by this chemical the effect is terrible and there is no antidote. They have trouble walking, muscle twitches, seizures, and high temperature. If not treated they can suffer a stroke and die within hours. "A flea treatment that people think will save money, can kill cats and end up being really costly for owners, emotionally and financially," Dr Lawrie said. "It's vital that if the box says DO NOT USE ON CATS, you should heed that warning. If you have a cat and dog you also need to be careful because the risk for your cat, even in accidental contact with a treated dog, is very high. "We would really like to see these treatments only made available through vets so that proper instructions could be given to each buyer and cats don't suffer unnecessarily. "If you have any questions or aren't sure which product to use, talk to your vet," Dr Lawrie said.

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<p>Australian Veterinary Association. (2008). "National permethrin toxicity campaign." Retrieved 24 August, 2009, from http://avacms.eseries.hengsystems.com.au/AM/Template.cfm?Section=Campaigns1&Template=/CM/HTMLDisplay.cfm&ContentID=10243.</p>	2008	Australia	<p>Permethrin is a pyrethroid insecticide found in some spot-on flea treatments for dogs. Spot-on flea treatments containing permethrin can cause severe toxicity in cats, which can result in convulsions and fatalities. In addition to direct application, cats are also at risk from secondary exposure through contact with other pets treated with a spot-on flea treatment that contains permethrin. In response to concerns raised by members about the number of permethrin toxicity cases in cats being treated, the AVA has launched a campaign to address the problem. Research currently underway by the Centre for Veterinary Education at the University of Sydney has so far found 431 cases in the last two years by surveying 130 practitioners. 122 of these cats died. Most of these cases are caused by spot-on treatments bought from supermarkets and pet shops where the owners haven't read the label warnings. The national campaign includes promoting research into the problem, looking at possible regulatory solutions, as well as raising awareness through the media and direct education campaigns to retailers. We have also approached the product manufacturers to raise our concerns. If you're a small animal practitioner, the campaign needs YOU! * If you haven't done it already, complete the Centre for Veterinary Education's survey about cases you have seen in the last two years. * When a cat comes for treatment, make sure you fill in the APVMA online adverse experience report. * If you're an AVA member and you get a case, raise awareness of the problem in your area through the local media. Contact the AVA Media Relations Manager, Juanita Feldbauer via email or on 02 9431 5062 for help making contact with your local radio stations and newspaper. * If you write an advice column for your local paper, use the warmer weather to raise awareness of the problem – while fine for dogs, these products can be lethal to cats, and owners must always read labels.</p>
<p>Barbier, N. (2005). Bilan d'activité du Centre National d'Informations Toxicologiques Vétérinaires pour l'année 2003. <u>Ecole Nationale Veterinaire de Lyon</u>. Docteur vétérinaire: 220.</p>	2005	France	<p>La majorité des 11,941 appels reçus en 2003 concerne les carnivores domestiques. Ils représentent en effet 86% des appels, les ruminants 5,4% et les équins 3,9%. Les interlocuteurs privilégiés du CNITV sont les vétérinaires praticiens, qui représentent 73% des appels, mais la proportion d'appels provenant des particuliers est en constante progression. Les pesticides représentent la classe de toxiques la plus importante pour la majorité des espèces (sauf pour les équins pour lesquels les plantes sont plus importantes), devant les médicaments qui ne concernent quasiment que les carnivores domestiques, les polluants et les plantes. PERMETHRIN (pages 94-97) Cats are more sensitive to the pyrethroids as illustrated by the disproportionate number of cats versus dogs presenting with intoxication. Amongst a large range of pyrethroids, the most commonly involved was permethrin. There were 88 cases of pyrethroid intoxication of cats, with approximately 80% described as moderate or severe when reported to the CNITV (cf dogs, 48% of 104 cases described as moderate or severe).</p>

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
Baynes, R. E. (2009). Ectoparasiticides. <u>Veterinary Pharmacology and Therapeutics</u> . J. E. Riviere and M. G. Papich. Ames, Iowa, Wiley-Blackwell: 1181-1202.	2009	USA	Pyrethrins and Synthetic Pyrethroids. Safety/toxicity (pages 1194-1195) "Dermal exposure to pyrethrins and pyrethroids rarely results in systemic absorption to cause significant signs of toxicity in domestic animals, but grooming of the treated hair coat by cats can result in significant oral ingestion of pyrethroids. Cats, more so than dogs, are presented with clinical signs of toxicity, and this is often after the dog formulation was inadvertently applied topically to adult cats or kittens or the untreated cats comes into physical contact with a treated dog. Recall that cats are deficient in their ability to clear chemicals by hepatic glucuronidation. This explains why cats are more sensitive than dogs to pyrethroids. The dog-only spot-on flea and tick products can contain as much as 45-65% permethrin, which at this concentration can be very harmful to most cats (Meyer 1999). Not only is permethrin toxicity in cats a great concern, but so is phenothrin toxicity in cats. Phenothrin, a Type 1 pyrethroid similar to permethrin, was originally approved as a spot-on product with 85.7% phenothrin for cats. These products were cancelled in 2005 by the manufacturer because of the adverse effects and numerous deaths in feline patients."
Beasley, V. R. (1993). "Pesticides and pets." <u>ACS Symposium Series</u> 522 : 344-351.	1993	USA	As compared to much older products containing "classical pesticides", such as the rodenticide warfarin and the insecticide carbaryl, many newer formulations are more hazardous to domestic animals in urban and suburban environments. Although progress has been marked in the area of insecticide baits for use in homes, at least one fly bait which is particularly lethal to dogs is still widely available. In the case of rodenticides, recent experience has reflected generally negative progress with regard to small animal safety. Indeed, some products relatively new to the marketplace routinely cause prolonged suffering, necessitate expensive and often ineffective therapies, and can induce permanent organ damage despite vigorous treatment of the inadvertently exposed pet animal.
Beasley, V. R. and H. L. Trammel (1989). Incidence of poisonings in small animals. <u>Current Veterinary Therapy X Small Animal Practice</u> . J. D. Bonagura. Philadelphia, W. B. Saunders Company: 97-113.	1989	USA	Pyrethrin and pyrethroid insecticides "In 1986, pyrethrin calls to the center with regard to cats were more numerous than for any other generic; over 60 per cent of these calls were regarded as toxicosis or suspected toxicosis. Six of the feline calls assessed as suspected toxicosis were accompanied by deaths. Dogs appear to be affected less often." Fenvalerate and DEET Cats were most often affected by exposure to Hartz Blockade which contained fenvalerate and DEET.
Beasley, V. R., D. C. Dorman, et al. (1990). Pyrethrum (pyrethrins) and pyrethroids. A system affected approach to veterinary toxicology. V. R. Beasley. Champaign, IL, Illinois Animal Poison Information Center: 111-116.	1990	USA	
Berny, P., F. Caloni, et al. (2009). "Animal poisoning in Europe. Part 2: Companion animals." <u>The</u>	2009	France	Among veterinary drugs, external parasiticides are the single most common cause of poisoning with many cases involving adverse reactions to pyrethroids, particularly

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
<u>Veterinary Journal In Press, Corrected Proof.</u>			permethrin in cats (Martin and Campbell, 2000), with cases reported from Belgium, France, Italy and Spain . Whilst pyrethrins are safe to use in cats at the correct dose, pyrethroids are not. Permethrin poisoning commonly occurred after the cat had either been overdosed or inappropriately treated with a product labelled for dogs, with occasional fatal outcomes (Barbier, 2005).
Bessant, C. (2008). "How poison centres can help in animal welfare campaigns." <u>Clinical Toxicology</u> 46 (5): 358-358.	2008	UK	
Bordeau, W. (2009). "Intoxications du chat par la perméthrine: rares mais graves." <u>Dépêche Vétérinaire</u> 1018 (24 au 30 janvier).	2009	France	Les intoxications par la perméthrine chez le chat sont rares et résultent essentiellement de l'application de spot-on commercialisé chez un chien sur un chat. Certains cas peuvent également survenir suite au contact proche et prolongé avec un chien récemment traité . Il n'existe aucun antidote et on ne peut réaliser qu'un traitement de soutien symptomatique.
Bottcher, I. C., H. C. Schenk, et al. (2006). "Permethrin intoxication in ten cats - retrospective evaluation." <u>Tieraerztliche Praxis Ausgabe Kleintiere Heimtiere</u> 34 (3): 185-+.	2006	Germany	Objective: The current study summarises clinical findings and treatment of cats with permethrin intoxication presented at the Small Animal Clinic of the University of Veterinary Medicine Hannover between 2002 and 2005. Material and methods: Ten cats were topically treated by their owners with a spot-on permethrin product designated for dogs. Signalement, signs, course of the disease and treatment are described. Results: Nine domestic shorthair cats and one siamese cat with a median age of 4.75 years and a median body weight of 5 kg were affected. The owners recognised the first signs after two to 24 hours. The median duration of symptoms was 30 hours and included tremor, mydriasis, generalised seizures, tachycardia, hyperthermia and ventricular extrasystoles. Treatment consisted of rinsing with detergents, clipping, maintenance of normal body temperature and treatment of seizures and tremor with diazepam, phenobarbital and/or pentobarbital. One animal was euthanised on the owner's request. The remaining nine cats were discharged without any symptoms after two to nine days. Conclusion and clinical relevance: With early and symptomatic treatment, prognosis of permethrin intoxication in cats is good.
Bough, M. (2000). "Permethrin toxicosis in cats." <u>Veterinary Technician</u> 21 (9): 506-507.	2000	USA	Permethrin is a synthetic type I pyrethroid insecticide that is used in an assortment of products from shampoos and sprays to topical canine spot-on products. Many spot-on flea products are available at discount, grocery, and farm stores. Made by various manufacturers, these products have become increasingly popular because of their ease of application and length of efficacy (generally 1 month). Many of these products contain 45% - 65% permethrin and are labelled for use on dogs only. When applied according to label instructions, spot-on products are generally safe and efficacious. However, when these products are used on animals contrary to those listed on the label instructions, toxicosis may result. Veterinary technicians should be educated about the clinical signs associated with permethrin toxicosis in cats as well as

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			treatment options. Some pet owners apply spot-on permethrin-containing insecticides on their cats without reading the manufacturer's label, whereas others may read the label but think that a small amount of the product is safe to use. Some cats are exposed to permethrin by coming into contact with dogs that have been treated with a spot-on product. Despite the source of exposure, the end result can be devastating.
Buck, W. B. (1995). Top 25 generic agents involving dogs and cats managed by the National Animal Poison Control Center in 1992. <u>Kirk's Current Veterinary Therapy XII Small Animal Practice</u> . J. D. Bonagura. Philadelphia, W. B. Saunders Company: 210.	1995	USA	There was a total of 5,351 cases involving one or more cats reported in 1992. Permethrin is listed as one of the top 25 agents reported in cats.
Campbell, A. and M. Chapman (2000). <u>Handbook of poisoning in dogs and cats</u> . Oxford ; Malden, MA :, Blackwell Science.	2000	UK	Pyrethrins and pyrethroids (pages 42-45) Since 1992 the London centre of the VPIS has received between 10 and 50 enquiries per annum regarding pyrethroids and pyrethrins in animals. Approximaetly 65% of these involve cats. Many of the feline cases arise as a result of dermal application of products intended for use in dogs. These products contain similar ingredients as the feline products but often in higher concentrations. "Cats are more susceptible to toxicity than dogs." Occasionally, toxicity may arise from animals being in close association or grooming treated animals. Similtaneous exposure to OPs may increase the toxicity of SPs.
Curti, R., J. Kupper, et al. (2009). "[A retrospective study of animal poisoning reports to the Swiss Toxicological Information Centre (1997 - 2006)]." <u>Schweiz Arch Tierheilkd</u> 151 (6): 265-73.	2009	Switzerland	The purpose of this retrospective study was to analyse the etiology, frequency and outcome of toxicological cases recorded by the consultation service of the Swiss Toxicological Information Centre (STIC) hotline over a 10-year period, from 1997 to 2006. A detailed analysis of this database indicates that common human drugs not intended for use in animals, as well as pesticides and toxic plants represent the most prominent hazards involved in the reported cases of animal poisonings. The comparison with a previous survey from the years 1976-1985 revealed new toxic risks due to the accidental uptake of cannabis products, castor seeds or chocolate by dogs. In addition, there is a striking increase of serious poisonings with permethrin in cats. The follow-up reports delivered by veterinarians also reflect novel pharmacological and technological trends in the management of poisonings.
Delhaye, D. (2008). Effets indésirables et intoxications dus à l'utilisation de médicaments à base de perméthrine chez le chat. Etude épidémiologique. Lyon, École Nationale Vétérinaire de Lyon. Docteur Vétérinaire : 151.	2008	France	RESUME Dans une première partie, un bilan bibliographique du mode d'action de la perméthrine est effectué, ainsi que des hypothèses passées et actuelles expliquant sa toxicité chez le chat. Une seconde partie présente d'abord les méthodes d'une enquête effectuée sur les circonstances des intoxications des chats par les médicaments contenant de la perméthrine et de leur traitement, ceci à partir des données de l'ANMV et du CPVL ; sont ensuite exposés les résultats de cette enquête. Enfin, est réalisée une étude de la présence de la contre-indication d'utilisation sur les chats sur les emballages, notices et RCP de ces médicaments, ainsi qu'un bilan de l'impact des

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			<p>mesures prises en mars 2003 par la commission de pharmacovigilance.</p> <p>CONCLUSION Nous avons vu, au cours de notre étude, à quel point les intoxications des chats par des antiparasitaires externes contenant de la perméthrine sont toujours d'actualité. Les laboratoires produisant ces antiparasitaires externes destinés aux chiens sont pourtant conscients de l'importance de ce problème, et modifient, parfois à l'encontre de ce qui leur est autorisé, leurs notices et leurs emballages afin d'informer le propriétaire de chat de la toxicité de la perméthrine chez cette espèce. Ils anticipent de cette manière les modifications des R.C.P., qui sont malheureusement très lentes à être mises en place. Cependant, il semble évident que ces informations de plus en plus détaillées ne permettent pas de diminuer de manière visible le nombre de chats intoxiqués chaque année par les antiparasitaires externes contenant de la perméthrine ; ceci s'expliquant par le fait que le propriétaire de chat, trouvant ces spécialités plus ou moins en libre-service dans divers lieux de vente, ne lit que très rarement la notice avant d'appliquer l'antiparasitaire sur le chat. Ainsi, les conclusions du rapport d'expertise de l'AFSSA, publié en mars 2003 n'ont pas permis, et ne permettront probablement pas, de réduire le nombre de ces intoxications parfois mortelles. Il apparaît donc nécessaire, si la profession vétérinaire souhaite disposer à l'avenir des nombreux avantages que présente cet antiparasitaire chez le chien, que le circuit de distribution des médicaments contenant de la perméthrine soit revu, ou dans le sens d'une formation approfondie des pharmaciens quant à la toxicologie de cette molécule, ou dans le sens d'une restriction des sites de vente de ces antiparasitaires aux structures vétérinaires seules. Dans tous les cas, il serait prudent de retirer de la vente en libre-service ces spécialités présentes dans les grandes surfaces et animaleries.</p>
Dorman, D. C. and J. D. Fikes (1993). "Diagnosis and therapy of neurotoxicological syndromes in dogs and cats - selected syndromes induced by pesticides .2." <u>Progress in Veterinary Neurology</u> 4 (4): 111-120.	1993	USA	This is the second of three articles discussing neurotoxic syndromes in companion animals. The first paper (published in the Fall 1993 issue of Progress in Veterinary Neurology) described the classification, diagnosis, and management of neurotoxicoses and provided a brief survey of those toxicants that primarily affect the nervous system. This paper will discuss several pesticide-induced neurotoxic syndromes in companion animals [including pyrethroid intoxication]. The last article in this series will focus on neurotoxicoses induced by metals. While a complete review of neurotoxicants is beyond the scope of this series, the authors will address certain commonly occurring neurotoxicologic syndromes of veterinary importance.
Dorman, D. C. and V. R. Beasley (1991). "Neurotoxicology of pyrethrin and the pyrethroid insecticides." <u>Veterinary and Human Toxicology</u> 33 (3): 238-243.	1991	USA	Natural pyrethrin and synthetic pyrethroid insecticides have been considered among the safest classes of insecticides available. Pyrethrins and pyrethroids are classified on the basis of their chemical structures and their toxicologic, neurophysiologic and pharmacologic effects. Cellular effects of pyrethrin and pyrethroid insecticides have been postulated to involve interactions with sodium channels, receptor-ionophore

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			complexes, neurotransmitters, and ATPases. Toxicity is a function of chemical structure, metabolism, route of exposure, and the presence or absence of synergists. Pyrethroid insecticides are neurotoxic, and the development and severity of clinical signs is proportional to the nervous tissue pyrethroid concentration. Type I pyrethroid poisoning in mice and rats produces a syndrome characterized by tremors, prostration and altered startle reflexes. Type II pyrethroid poisoning in mice and rats causes ataxia, convulsions, hyperactivity, choreoathetosis and profuse salivation. A presumptive diagnosis of pyrethrin/pyrethroid poisoning is based upon history of exposure, development of appropriate clinical signs, and chemical analysis for insecticide residues. Treatment of pyrethrin and pyrethroid toxicosis involves basic life support, seizure control when needed, and the prevention of further insecticide absorption.
Dorman, D. C., W. B. Buck, et al. (1990). "Fenvalerate/N,N-diethyl-m-toluamide (Deet) toxicosis in two cats." <u>Journal of the American Veterinary Medical Association</u> 196 (1): 100-2.	1990	USA	Toxicosis attributable to fenvalerate and N,N-diethyl-m-toluamide (Deet) exposure was suspected in 2 cats. Clinical signs of toxicosis developed within 4 to 6 hours of dermal application of the pesticide. Clinical signs of toxicosis seen in both cats included hypersalivation, ataxia, and depression. In addition, seizures were seen in 1 cat. Both cats died. Analysis of skin, kidney/urine, liver, and brain tissues confirmed the presence of fenvalerate and Deet. The pyrethroid fenvalerate and the insect repellent Deet are used for the control of fleas and ticks on cats. Suspected fenvalerate/Deet toxicosis in cats is associated with tremors, hypersalivation, ataxia, vomiting, depression, and seizures.
Durand, F. (1993). Risques toxiques des insecticides pyrethroides pour les carnivores domestiques etude epidemiologique d'apres les cas du centre antipoison veterinaire de lyon (1990-1992). <u>Ecole Nationale Veterinaire de Lyon</u> . Lyon, Université Claude Bernard. Doctorat vétérinaire : 139.	1993	France	Les pyrethroides forment une famille d'insecticides de toxicite importante pour les animaux a sang froid et meconnue pour les homeothermes. le CNITV-Lyon a enregistre sur une periode de trois ans 345 cas d'intoxications certaines de chiens et de chats par les pyrethroides. Leurs risques toxiques sont reevalues. L'etude de ces intoxications a permis d'analyser leurs circonstances afin de mieux les prevenir.
Dyer, F., E. Brown, et al. (2009). "Suspected adverse reactions, 2008." <u>Veterinary Record</u> . 165 (6): 162-164.	2009	UK	
Dyer, F., M. Spagnuolo-Weaver, et al. (2006). "Suspected adverse reactions, 2005." <u>Veterinary Record</u> . 158 (14): 464-466.	2006	UK	PERMETHRIN Of the 86 cases resulting from use in an unauthorised species, 64 (74.4 per cent) occurred in cats, representing a decrease of 19 in this species compared with 2004. The incidence of adverse reactions in cats resulting from the unauthorised use of canine 'spot-on' products containing permethrin showed a corresponding decrease, from 0.0022 per cent in 2004 to 0.0013 per cent in 2005.
Dyer, F., M. Spagnuolo-Weaver, et al. (2007). "Suspected adverse reactions, 2006." <u>Veterinary Record</u> . 160 (22): 748-750.	2007	UK	PERMETHRIN Of the 89 cases resulting from use in an unauthorised species, 77 (83.7%) occurred in cats, representing an increase of 13 in this species compared with 2005. The incidence of adverse reactions in cats resulting from the unauthorised use of

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			canine 'spot-on' products containing permethrin showed a corresponding increase, from 0.0013 per cent in 2005 to 0.0021 per cent in 2006.
Dyer, F., M. Spagnuolo-Weaver, et al. (2008). "Suspected adverse reactions, 2007." <u>Veterinary Record</u> 163 (3): 69-72.	2008	UK	PERMETHRIN Of the 77 cases resulting from use in an unauthorised species, 63 (81.8%) occurred in cats, representing a decrease of 14 in this species compared with 2006. The incidence of adverse reactions in cats resulting from the unauthorised use of canine 'spot-on' products containing permethrin decreased from 0.0021 per cent in 2006 to 0.0017 per cent in 2007.
Dymond, N. L. and I. M. Swift (2008). "Permethrin toxicity in cats: a retrospective study of 20 cases." <u>Australian Veterinary Journal</u> 86 (6): 219-223.	2008	Australia	Objective Permethrin is a synthetic pyrethroid widely used in flea control products for small animals. Accidental toxicity can occur with off-label usage, and cats are particularly susceptible. Methods Retrospective study of 20 cases of permethrin toxicity in cats treated at an emergency clinic in Brisbane, Queensland from October 2004 to June 2005. Results The diagnosis of permethrin toxicity was made on the basis of a history of exposure and characteristic clinical signs, including seizures, muscle fasciculations, and tremors. Decontamination and appropriate seizure or muscle fasciculation control were the basis of treatment. The outcome was good after rapid intervention and 19 of the 20 cats were successfully treated, with the only death occurring in a kitten for which treatment was delayed for 24 h. No long-term complications were reported by the cats' owners at 4-month follow-up after discharge from hospital. Conclusions Owner education, together with more appropriate product labelling, may help eliminate this problem in the future.
Ensley, S. (2007). Pyrethrins and pyrethroids. <u>Veterinary Toxicology</u> . Oxford, Academic Press: 494-498.	2007	USA	Summary Pyrethrins are the insecticidal compounds obtained from the flowers of the plant <i>Tanacetum cinerariaefolium</i> , also called <i>Chrysanthemum cinerariaefolium</i> or <i>Pyrethrum cinerariaefolium</i> . Pyrethrum denotes extracts from the flowers that contain the active pyrethrin compounds (Proudfoot, 2005). The use of pyrethrum in insecticide preparations dates back to Persia, about 400 BC Pyrethroids are synthetic analogs of pyrethrins. Because of stability problems with the natural pyrethrins, these insecticides were replaced by the more stable organophosphate and organochlorine insecticides developed after World War II (Valentine, 1990). As a result of the toxicity and environmental contamination associated with the organophosphate and organochlorine insecticides, interest in the use of pyrethrins and pyrethroids re-emerged in the 1970s. Pyrethrin and pyrethroid insecticides are effective against a variety of insect pests on companion animals and livestock, and are used on farms, in the home and garden and have many public health applications because of the safety associated with these compounds.
Fitzgerald, K. T., A. C. Bronstein, et al. (2006). "'Over-the-counter' drug toxicities in companion animals." <u>Clin Tech Small Anim Pract</u> 21 (4): 215-26.	2006	USA	A truly astonishing variety of "over-the-counter" drugs not taken under the auspices of a physician or veterinarian and not regulated by the Federal Drug Administration (FDA) are currently available to the American public. Many of these are widely advertised, readily available, remarkably inexpensive, and universally taken. Although most of the

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			over-the-counter medications are fairly safe, the potential for toxic episodes exists due in large part simply on account of the amounts curious unsupervised animals may ingest. Another part of the problem is that since they are over the counter a large proportion of the public perceives them as totally harmless. In this article, we will investigate the most frequently seen non-prescription intoxications, their mechanism of action, clinical signs, diagnosis management, and prevention.
Gfeller, R. W. and S. P. Messonnier (2004). <u>Handbook of small animal toxicology and poisoning</u> . St Louis, Mosby.	2004	USA	Pyrethrins/pyrethroids, pp282-286
Gleadhill, A. (2004). "Permethrin toxicity in cats." <u>Veterinary Record</u> 155 (20): 648.	2004	UK	
Gray, A. (2000). "Permethrin toxicity in cats." <u>Veterinary Record</u> 147 (19): 556-556.	2000	UK	
Gray, A. (2001). "Permethrin toxicity in cats following use of canine permethrin spot-on products." <u>Veterinary Record</u> 149 (21): 660.	2001	UK	
Hall, K. (2008). Toxin exposures and treatments: a survey of practicing veterinarians. <u>Kirk's current veterinary therapy XIV</u> . J. D. Bonagura and D. C. Twedt. Philadelphia, Pa, Elsevier Saunders: 95-99.	2008	USA	The results of a survey of veterinarians on common small animal toxin exposures and treatments conducted by the University of Minnesota and the Veterinary Information Network is presented. In response to the question "the five most common toxin exposures in CATS that present to my practice are", 86% of respondents listed pyrethrin/permethrin. Other exposures listed in decreasing rank order were plant intoxication (66%), ethylene glycol (47%), acetaminophen (42%), animal envenomation (40%), NSAIDs (39%), human prescription medication (34%), anticoagulant rodenticides (27%), and cholinesterase inhibitors (9%). In response to the question "the five most common toxin exposures in DOGS that present to my practice are" the following rank order of exposures was collected: anticoagulant rodenticides (89% of respondents), chocolate (54%), animal envenomation (51%), NSAIDs (45%), human prescription medication (45%), ethylene glycol (32%), plant intoxication (22%), pyrethrin/permethrin (22%), drugs of abuse (eg marijuana, cocaine) (18%) and metaldehyde (snail bait) (16%).
Hansen, S. R. (1995). Management of adverse reactions to pyrethrin and pyrethroid insecticides. <u>Kirk's Current Veterinary Therapy XII Small Animal Practice</u> . J. D. Bonagura. Philadelphia, W. B. Saunders Company: 242-245.	1995	USA	No mention that cats are especially sensitive to permethrin or other SPs. "Overapplication of products on cats is more likely to result in adverse reactions because cats have a greater surface area/bodyweight ratio, making it easier to overdose a small pet but difficult to overdose a large pet."
Hansen, S. R. (2001). Pyrethrins and pyrethroids. <u>Small animal toxicology</u> . M. E. Peterson and P. A. Talcott. Philadelphia :, Saunders: 687-694.	2001	USA	Toxic doses for pyrethrin and pyrethroid compounds vary substantially and in most cases are not known for dogs or cats. "One specific toxicosis warrants special comment. Based o the public database of the American Society for the Prevention of

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			<p>Cruelty to Animals (ASPCA) National Animal Poison Control Center, "spot-on" products that contain the pyrethroid permethrin, which are labeled clearly for use on dogs only, result in serious toxicosis when used inappropriately in cats. Significant adverse reactions in dogs are rare. Based on these cases, dermal application of 100mg/kg permethrin (1mL of 45% permethrin applied dermally to a 4.5-5kg cat), if untreated, can result in life-threatening toxicosis. The minimum toxic dose is unknown, but would be expected to be significantly lower. Base on data from these and other cases, cats are exceptionally sensitive to permethrin compared to dogs or rats. In general, cats are more sensitive than most other species to pyrethrin, pyrethroid, and other insecticides." "Products formulated for cats should contain less than 0.20% permethrin." Case report from ASPCA NAPCC database: A 1-year-old 4.5kg castrated male domestic shorthair cat was presented to an emergency clinician. The owner of the cat has applied a 1-mL 45% permethrin, 5% pyriproxyfen (Nylar) "spot-on" product that is registered for use only on dogs. Within 4 hours of exposure the cat developed hypersalivation, severe tremors and seizures. Various interventons (including diazepam, methocarbamol and pentobarbital) did not control seizures and the owner elected to have the cat euthanized.</p>
<p>Hansen, S. R. (2006). Pyrethrins and pyrethroids. <u>Small animal toxicology</u>. M. E. Peterson and P. A. Talcott. Philadelphia :, Saunders: 1002-1010.</p>	2006	USA	<p>Toxic doses for pyrethrin and pyrethroid compounds vary substantially and in most cases are not known for dogs or cats. "One specific toxicosis warrants special comment. Based o the public database of the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center, "spot-on" products that contain the pyrethroid permethrin, which are labeled clearly for use on dogs only, result in serious toxicosis when used inappropriately in cats. Significant adverse reactions in dogs are rare. Based on these cases, dermal application of 100mg/kg permethrin (1mL of 45% permethrin applied dermally to a 4.5-5kg cat), if untreated, can result in life-threatening toxicosis. The minimum toxic dose is unknown, but would be expected to be significantly lower. Base on data from these and other cases, cats are exceptionally sensitive to permethrin compared to dogs or rats. In general, cats are more sensitive than most other species to pyrethrin, pyrethroid, and other insecticides." "Products formulated for cats should contain less than 0.20% permethrin." Phenothrin - some cats appear sensitive to properly registered EPA approved spot-on formulations containing 85.7% phenothrin. Production of such products ended September 30 2005 and sales were discontinued by March 31 2006. Case report 1 from ASPCA NAPCC database: A 1-year-old 4.5kg castrated male domestic shorthair cat was presented to an emergency clinician. The owner of the cat has applied a 1-mL 45% permethrin, 5% pyriproxyfen (Nylar) "spot-on" product that is registered for use only on dogs. Within 4 hours of exposure the cat developed hypersalivation, severe tremors and seizures. Various interventons (including diazepam,</p>

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			methocarbamol and pentobarbital) did not control seizures and the owner elected to have the cat euthanized. Case report 2 A 5-year-old, 6.8 kg castrated male domestic shorthair cat was treated by its owner with 2.5mL 44% permethrin, 8.8% imidacloprid spot-on product registered by the EPA for use only on dogs. Within 2.5 hours the cat was exhibiting muscle tremors, was hyperthermic (103degF) and vomited. Within 4 hours of exposure the cat was bathed to decontaminate the skin and hair coat and administered methocarbamol. The cat fully recovered. The cat was exposed to 162mg/kg permethrin and 32mg/kg imidacloprid.
Hansen, S. R. and W. B. Buck (1992). "Treatment of adverse reactions in cats to flea control products containing pyrethrin/pyrethroid insecticides." <u>Feline Practice</u> 20 (5): 25-27.	1992	USA	Refers to products labelled for cats. No mention of special sensitivity of cat to permethrin. "Frequent or heavy spraying of cats with topical products increases the likelihood of toxicity. In other situations, over-application of premise products in the house or direct application of premise products to the cat may induce toxicosis. It is important to keep the cat out of a treated house until the area has been allowed to completely dry." Clinical signs and treatment recommendations (including use of methocarbamol). Concluded that "most cats recover following topical exposure to natural pyrethrins within 24-38 hours; however, longer periods of treatment may be required."
Hansen, S. R., K. A. Stemme, et al. (1994). "Pyrethrins and pyrethroids in dogs and cats." <u>Compendium on Continuing Education for the Practicing Veterinarian</u> 16 (6): 707-712.	1994	USA	Pyrethrin insecticides are derived from <i>Chrysanthemum cinerariaefolium</i> and related species; pyrethroid insecticides are synthetic analogues of pyrethrins. Both compounds are commonly incorporated in flea and tick control products for dogs and cats. Pyrethrin and pyrethroid insecticides reversibly increase the sodium conductance of nerves, resulting in repetitive nerve discharges. Misuse or overuse of topical pyrethrin products or use on an unusually sensitive dog or cat can produce clinical signs. "Cats are more sensitive to topical permethrin than dogs." (page 709)
Hornfeldt, C. S. and M. J. Murphy (1992). "1990 report of the American Association of Poison Control Centers: poisonings in animals." <u>Journal of the American Veterinary Medical Association</u> 200 (8): 1077-80.	1992	USA	Brief review of 41,854 animal exposure cases reported to the National Data Collection System by 47 of 72 participating poisons centres. Pyrethrins were associated with 6 (1.4% of total) deaths, but species involved is not stated.
Hovda, L. R. (2008). Toxin exposures in small animals. <u>Kirk's current veterinary therapy XIV</u> . J. D. Bonagura and D. C. Twedt. Philadelphia, Pa, Elsevier Saunders: 92-94.	2008	USA	A brief summary is presented of the more than 9,000 calls received by the Pet Poison Helpline (PPH) (a division of SafetyCall International that began fee-for-service animal toxicology and poison information in 2004) in the 12-month period from 1 July 2005 to 30 June 2006. About 88% of the calls involved young dogs followed by cats and a variety of other species. The majority of calls originated from the caller's home, generally had no to few clinical signs and were treated at home with no referral to a health care facility. Clinical effects in dogs were usually mild and the outcome was excellent. Cats, however, seemed to have a more difficult time and the outcome was not as good. Dogs and cats were equally represented in calls involving veterinary

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			products. Topical flea and tick products, including pyrethrin-based products, showed a seasonal occurrence. "Clinical signs and outcomes were worse with pyrethrin-based flea products, especially in cats."
Keck, G. (2003). Effets indésirables des spécialités antiparasitaires externes à base de perméthrine utilisées en « spot-on » chez les carnivores domestiques. Rapport d'expertise de pharmacovigilance relatif à l'avis CNPV – 01 du 18/03/2003. ANMV, AFSSA. Fougères, Commission Nationale de Pharmacovigilance Vétérinaire.	2003	France	Conclusion : Sur la période de l'étude (01/01/01 au 30/09/02), 610 notifications ont été recueillies par les deux centres de pharmacovigilance vétérinaire et par l'AFSSA agence nationale du médicament vétérinaire pour un nombre total de 3,198,087 pipettes vendues, ce qui représente environ 0.19 cas pour 1,000 pipettes vendues ; 1. Le nombre d'effets indésirables rapporté au chiffre de vente est comparable pour les 4 spécialités étudiées quel que soit le circuit de distribution (vétérinaire ou pharmacien) ; 2. les 110 cas notifiés relatifs aux chiens ne représentent que 18% des notifications enregistrées, soit environ 0.03 cas d'effets indésirables déclarés pour 1,000 pipettes vendues ; les symptômes chez le chien correspondent à des cas non graves ; 3. les 500 autres cas notifiés sont observés chez le chat, espèce pour laquelle la perméthrine est contre-indiquée par l'autorisation de mise sur le marché ; les 42 cas de mortalité (survenus) notifiés chez le chat correspondent environ à 0.01 cas pour 1,000 pipettes vendues bien qu'il soit impossible de connaître le nombre précis de chats traités. 4. les indications et contre-indications qui figurent sur les conditionnements sont globalement explicites avec cependant une lisibilité différente d'une spécialité à une autre. Elles méritent d'être uniformisées et renforcées.
Keck, G. (2003). Mesures à prendre pour faire cesser les effets indésirables des spécialités antiparasitaires externes à base de perméthrine utilisées en « spot-on » chez les carnivores domestiques. AVIS CNPV – 01 du 18/03/2003. Fougères, Commission Nationale de Pharmacovigilance Vétérinaire.	2003	France	La Commission : - recommande la mise en place d'une campagne d'information par les exploitants concernés auprès des distributeurs au détail, pharmaciens et vétérinaires, pour les sensibiliser à la nécessité d'informer les futurs utilisateurs de la contre-indication absolue concernant le chat et de la conduite à tenir en cas de problème ; - préconise une amélioration de la lisibilité des emballages pour la contre indication relative au « chat » qui doit être rendue encore plus explicite et homogène pour les différentes spécialités avec en particulier l'utilisation d'une très forte symbolique et d'une taille de caractères identique et suffisamment grande ; - suggère que des mentions supplémentaires relatives aux effets indésirables susceptibles d'être observés chez le chat [« peut entraîner des convulsions pouvant être mortelles »] et à la conduite à tenir si des effets indésirables surviennent chez le chat [« Laver le chat avec un shampoing ou de l'eau savonneuse. Consulter rapidement votre vétérinaire traitant. »] soient ajoutées sur l'étiquetage extérieur et, le cas échéant, la notice.
Kolf-Clauw, M. and V. Poletti (1998). "Main drug poisoning in domestic carnivores Pyrethroid parasiticide overdose." <u>Point Veterinaire</u> 29 (188): 56-62.	1998	France	One to six hours after a massive administration of pyrethroids, nervous and digestive problems occur, which then usually evolve favourably. These parasiticides are especially toxic in the cat and small dogs. Overdose is the main cause of poisoning. Treatment should be symptomatic as well as help enhance term elimination. Prevention entails informing the owner on the usage of the parasiticide (6 figures, 3 tables, 21 references).

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
Lande, B. (1998). "Two cats poisoned with Coopersect vet. [deltamethrin]." <u>Norsk Veterinaertidsskrift</u> 110 (3): 145-146.	1998	Norway	A farmer who had applied Coopersect vet. (deltamethrin) to his sheep, also applied it to 2 cats, placing about 5 ml between the shoulder blades. The cats were thought to have licked themselves and, after about an hour, were seen in convulsions, associated with salivation, urination and defaecation. Diazepam at 1 mg/kg body i.v. followed by repeated administration of Zoletil "cocktail" (tiletamine, zolazepam, xylazine and butorphenol) led to complete recovery in about 48 h. A brief review of pyrethroids, with toxicological information, is presented.
Linnett, P. J. (2008). "Permethrin toxicosis in cats." <u>Australian Veterinary Journal</u> 86 (1-2): 32-35.	2008	Australia	A retrospective analysis of all adverse experience reports received by the Australian Pesticides and Veterinary Medicines Authority's Adverse Experience Reporting Program for veterinary medicines since 1995, showed that permethrin toxicity in cats usually occurred after the owner applied a canine permethrin-containing product, typically a spot-on. Cats are also at risk from grooming or being in direct contact with recently treated dogs. This paper reviews permethrin toxicosis and its treatment in cats, incorporating information from the Australian and selected overseas veterinary pharmacovigilance programs.
Lorgue, G., J. Lechenet, et al. (1996). <u>Clinical veterinary toxicology</u> . Cambridge, MA, Blackwell.	1996	France	Pyrethroids (pages 163-164) No mention of pyrethroid toxicity to cats (animals most affected by pyrethroids listed as fish, dogs, cattle)
Macdonald, J. M. (1995). "Flea Control: An Overview of Treatment Concepts for North America." <u>Veterinary Dermatology</u> 6 (3): 121-130.	1995	USA	The approach to flea control emphasizes the importance of interrelationships between veterinarian and pet owner requiring knowledge of the unique environment of individual cases. A review of common parasiticides is briefly presented listing active ingredients and their classification. Concepts of developing a flea control program are presented that include aspects of inside and outside flea control as well as products and methods used to treat the pet. Newer products used in flea control are reviewed including insect growth regulators, insect development inhibitors, nematode treatment and borate compounds. [Their [pyrethroid]s toxicity is generally the same as pyrethrins, although some may have specific species toxicity. More concentrated formulations may increase the toxicity. This is evident with some some permethrin-containing products and variable toxicity to cats based on concentration and formulation.][Permethrin in certain products and concentrations may be toxic to cats and should only be used if labeled for that species.]
Malik, R. (2008). "Permethrin intoxication." <u>Australian Veterinary Journal</u> 86 (10): 373-373.	2008	Australia	
Malik, R., M. P. Ward, et al. "Permethrin Spot-On intoxication of cats: a review of the literature and a survey of veterinary practitioners in Australia." <u>Journal of Feline Medicine & Surgery</u> Submitted, uncorrected manuscript .	2009	Australia	A questionnaire was sent to veterinarians in Australia to determine the approximate number of cats presented for permethrin intoxication over a two-year period. Of the 269 questionnaires returned, 255 were eligible for analysis. A total of 207 respondents (81 per cent) reported seeing cases of permethrin spot-on intoxication (PSO) in cats over the last two years. A total of 750 individual cases were reported with 166 deaths. Although deaths were generally attributable to intoxication per se, in 39 cases cats

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			<p>were euthanased because owners were unable to pay anticipated treatment costs. Brands of PSO commonly implicated were Exelpet® (114 respondents), Advantix® (48) and Purina® (19), although 67 respondents were not able to identify a specific product. PSO formulations were most commonly obtained from supermarkets (146 respondents), followed by pet stores (43), veterinary practices (16), and a range of other outlets including produce stores and friends. The majority of cases involved PSOs labelled for use in dogs with specific label instructions such as "Toxic to cats". Owners applied PSO products accidentally or intentionally. Factors leading to accidental or intentional administration are discussed. In some cases, exposure was through secondary contact, such as when a PSO product was applied to a dog with which a cat had direct or indirect contact. It is the view of the authors that because of the likelihood of inappropriate use and toxicity in the non-labelled species, over-the-counter products intended for use in either dogs or cats must have a high margin of safety in all species. We argue that PSOs should only be available at points of sale where veterinary advice can be provided and appropriate warnings given. As interim measures, modified labelling with more explicit warnings may reduce morbidity and mortality.</p>
<p>Marsella, R. (1999). "Advances in flea control." <u>Veterinary Clinics of North America: Small Animal Practice</u> 29(6): 1407-1424.</p>	1999	USA	<p>Pyrethroids or synthetic pyrethrins (page 1408-1409). Cats are sensitive to the toxicity of pyrethroids, as the feline liver is inefficient at glucuronide conjugations relative to other mammalian livers. Permethrin at high concentration is extremely toxic to cats, and most products approved for this species contain 0.05% to 0.1% permethrin. Clinical signs of toxicity in cats depend on the type of pyrethroid that has been used and include ear flicking, paw shaking, hyper salivation, depression, muscle tremors, vomiting, anorexia, seizures, and possibly death.</p>
<p>Martin, A. and A. Campbell (2000). "Permethrin toxicity in cats." <u>Veterinary Record</u> 147(22): 639.</p>	2000	UK	
<p>Mensching, D. and P. A. Volmer (2007). Neurotoxicity. <u>Veterinary Toxicology</u>. R. C. Gupta. Oxford, Academic Press: 129-144.</p>	2007	USA	<p>Sodium Channels - pyrethroids (page 140) "Cats are most commonly presented to the veterinarian as a result of exposure to the highly concentrated (45–65%) spot-on permethrin products labeled for use in dogs. Within 12–18h of application or accidental exposure, affected cats will exhibit hyperesthesia, generalized tremors, hyperthermia, seizures, and possible death. The prognosis for complete recovery, however, is excellent provided that appropriate care is administered including control of tremors with IV methocarbamol, decontamination with a warm bath using a liquid dishwashing detergent, thermoregulation, seizure management (with diazepam, barbiturates, propofol, and/or inhalant anesthetics), and supportive care. The body temperature may become critically elevated with continued tremors and seizures or subnormal following a bath. Secondary adverse effects due to hyperthermia and enhanced toxicosis of pyrethroids at lower body temperatures may complicate the clinical course and should</p>

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
Merola, V. and E. Dunayer (2006). "The 10 most common toxicoses in cats." <u>Veterinary Medicine</u> 101 : 339–342.	2006	USA	be avoided." NUMBER ONE. Canine permethrin insecticides The topical application of a permethrin spot-on or dip product labeled for use only in dogs can lead to tremors and seizures in cats. These products, which generally contain 45% or 65% permethrin in spot-ons and 3% or more permethrin in dips, are applied to cats accidentally or by individuals who ignore the warnings on the label. In some instances, cats have developed signs of permethrin toxicosis after being in close contact with (sleeping near or grooming) a dog recently treated with a permethrin spot-on product. Initial signs may appear within a few hours but can take 24 to 72 hours to manifest. Fullbody tremors are the most common finding, although seizures may also occur. ¹ Other pyrethroids, including phenothrin and etofenprox , can cause a similar syndrome in cats when used at high concentrations. Treatment consists of bathing the cat in a liquid hand dishwashing detergent (e.g. Dawn Dishwashing Liquid— Procter & Gamble) to remove the sebum in which the product is distributed. If the cat is symptomatic, delay the bath until the tremors have been controlled. The tremors are best treated with slow intravenous boluses of methocarbamol (Robaxin-V—Fort Dodge Animal Health; total initial dose 55 to 220 mg/kg). ¹ Repeat the methocarbamol as needed, but do not exceed a dose of 330 mg/kg/day or respiratory depression may occur. ³ If methocarbamol is not effective, then barbiturates, propofol, or both can be used. Diazepam is generally ineffective for the tremors but should be used if seizures are present. Additional care should include monitoring the patient’s body temperature and administering intravenous fluids to protect the kidneys from myoglobinuria due to muscle breakdown. Atropine is not antidotal for permethrin; no true antidote exists. The prognosis is generally good with aggressive supportive care.
Meyer, E. K. (1999). "Toxicosis in cats erroneously treated with 45 to 65% permethrin products." <u>Journal of the American Veterinary Medical Association</u> 215 (2): 198-203.	1999	USA	Article describes reports of permethrin toxicosis due to PSOs in cats received by the USP Veterinary Practitioners Reporting Program (VPRP) and the EPA Incident Data System. Treatment recommendations and suggestions for reducing the incidence of this preventable toxicosis are discussed. USP VPRP Instances of misuse on cats were not reported to the USP before August 1997. Between August 1997 and September 1998 11 reports of PSO intoxication involving 12 cats were received, with 4 cats dying. One report of intoxication involved secondary exposure of a cat to two dogs treated 48 hours previously. EPA Incident Reports Between January 1994 and August 1998, 95 reports of PSO intoxication involving 125 cats were included in the EPA incident report summary. 33 cats were reported to have died, 41 cats were reported to have recovered and the final outcome of 51 cats is unknown. In addition there were 21 cases involving 24 cats believed to be the result of secondary exposure to treated dogs: 12 reports of cats that groomed treated dog; 5 cats in same house as treated dog; 2 cats slept with treated dog; 1 cat played with treated dog; 1 cat jumped on the back of a treated dog.

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			6 cats died, 7 recovered and outcome not known for 11. Scope of the problem "It is impossible to determine the true incidence of this problem; however, it is likely the described reports represent a small portion of the actual numbers of toxicoses. However, even if only the reported cases in this article are considered, it is clear that misuse of concentrated permethrin spot-on products is occurring in cats and causing preventable morbidity and mortality." Contributing factors "To develop strategies to reduce inappropriate use of permethrin spot-on products in cats, the circumstances facilitating this error must be identified. On the basis of discussions with veterinary practitioners and reports from owners, factors that may have contributed to the erroneous application of permethrin to cats include: the availability of permethrin spot-on products through non-veterinary sources, insufficient package warnings, and similar packaging of dissimilar products." Regulatory efforts Label improvements and post marketing surveillance described. Conclusion "It is hoped the industry, the EPA, the veterinary community, and pet owners can work together to eliminate the suffering and loss of life caused by the misuse of concentrated permethrin spot-on products on cats."
Meyer, E. K. (2000). "Toxicosis in cats erroneously treated with 45 to 65% permethrin products (vol 215, pg 198, 1999)." <u>Journal of the American Veterinary Medical Association</u> 216 (8): 1287-1287.	2000	USA	
Mount, M. E., G. Moller, et al. (1991). "Clinical illness associated with a commercial tick and flea product in dogs and cats." <u>Vet Hum Toxicol</u> 33 (1): 19-27.	1991	USA	A commercial flea and tick product containing 9.0% fenvalerate for use in dogs and cats was suspected of causing illness. An acute toxicity study was performed in 10 dogs and 10 cats exposed to the product orally (po) and dermally at differing doses. Samples were obtained for DEET and fenvalerate analysis. Oral dosing of dogs and cats produced severe clinical illness at doses as low as 0.66% of a can (7 ounce spray can)/kg body weight. Dermal application of the product resulted in minor clinical abnormalities in dogs. Oral exposure at 0.5% can/kg body weight resulted in severe illness, and dermal application caused severe illness or death in cats at 20% and 40% of a can/kg body weight. The cats receiving 10% of a can/kg body weight dermally became depressed for several hours but recovered uneventfully. Serum DEET concentrations closely paralleled the clinical signs observed in the animals. Serum concentrations of DEET above 20 ppm were considered diagnostic for intoxication. Urine concentrations of DEET above 1 ppm and tissue (liver, bile, and kidney) concentrations of DEET above 10 ppm were supportive of poisoning; values near 100 ppm were diagnostic for fatal poisoning.
Muguet-Chanoit, A. (2007). "Intoxication du chat à la perméthrine: prévenir et traiter." <u>Dépêche Vétérinaire</u> 955 (22 septembre au 28 septembre).	2007	France	La perméthrine est un neurotoxique très agressif chez le chat. Etant donné le nombre important d'intoxications annuelles, la prévention et l'avertissement des propriétaires ne semblent pas assez pratiqués par les vendeurs de ces traitements antiparasitaires.

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
Muntener, C. R., L. Bruckner, et al. (2007). "Declaration of suspected adverse reactions for veterinary drugs and vaccines in 2005." <u>Schweizer Archiv Fur Tierheilkunde</u> 149 (2): 57-63.	2007	Switzerland	We received 105 reports of suspected adverse events (SARs) following the use of veterinary drugs for the year 2005. This corresponds to a 35% increase compared to 2004. Practicing veterinarians sent most of these declarations. 73% of these concerned drugs used on companion animals. Antiparasitic drugs approved for topical use were the most frequently represented group with 48%, followed by drugs used to treat gastrointestinal disorders (11%) and drugs used off label (14%; other target species or other indication). For the first time 2 declarations concerning the application of permethrin containing spot-on preparations used by mistake on cats were received. An overview of 20 declarations about adverse reactions following application of different vaccines is also presented with emphasis on the problem of fibrosarcoma in cats. We are pleased by the growing interest shown by practicing veterinarians for the vigilance system and hope, to further develop this collaboration in the future.
Murphy, M. J. (1994). "Toxin exposures in dogs and cats - pesticides and biotoxins." <u>Journal of the American Veterinary Medical Association</u> 205 (3): 414-421.	1994	USA	Brief mention of pyrethrins and pyrethroids as sources of intoxication in dogs and cats. No mention that cat may be particularly sensitive. Supportive treatment may include diazepam.
Nebbia, C. (2009). "Pyrethroids are not the most appropriate remedy for tackling fleas and ticks in cats, and may be dangerous for fish too." <u>The Veterinary Journal</u> 182 (1): 1-2.	2009	Italy	
Nicholson, S. S. (2000). Toxicology. <u>Textbook of Veterinary Internal Medicine. Diseases of the dog and cat</u> . S. J. Ettinger and E. C. Feldman. Philadelphia, W. B. Saunders Company. 1 : 357-363.	2000	USA	Pyrethrin and pyrethroid insecticides (page 359) "Cats appear to be more susceptible to pyrethroid poisoning than dogs."
Page, S. W. (2008). Antiparasitic drugs. <u>Small Animal Clinical Pharmacology</u> . J. E. Maddison, S. W. Page and D. B. Church. Edinburgh, Elsevier, Second Edition: 198-269.	2008	Australia	Permethrin (page 236) "...in contrast to low potential for toxicity in most mammals ... cats are very sensitive to permethrin ...". Permethrin intoxication in cats is manifested principally by hyperexcitability, tremors and seizures. Cats exposed to high-concentration permethrin products with delayed initiation of treatment are at increased risk of death.
Platt, S. R. and N. J. Olby (2004). Neurological emergencies. <u>BSAVA manual of canine and feline neurology</u> . S. R. Platt and N. J. Olby. Gloucester, British Small Animal Veterinary Association: 333-335.	2004	UK	
Plumb, D. C. (2008). <u>Plumb's veterinary drug handbook</u> . Sixth edition. Stockholm, Wisconsin, PharmaVet (Distributed by Blackwell Publishing, Ames, Iowa).	2008	USA	PERMETHRIN Imidacloprid with permethrin, topical (Page 1009) The combination product with permethrin (K9 Advantix 8.8% imidacloprid, 44% permethrin) must not be used on cats. Use with caution in households with both dogs and cats, particularly if cats are in close contact or will groom dogs in the household. Permethrin (Page

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			1012-1013) Permethrin (and other synthetic pyrethroids can be toxic to cats, particularly small kittens. Only use products containing pyrethroids labeled for use on cats on this species.
Pouliquen, H. (2003). "Pyrethrinoid poisoning in cats and dogs." <u>Point Veterinaire</u> 34 (235): 38-41.	2003	France	
Richardson, J. A. (2000). "Permethrin spot-on toxicoses in cats." <u>Journal of Veterinary Emergency and Critical Care</u> 10 (2): 103-106.	2000	USA	Spot-on insecticides are becoming a popular type of flea control for pets. Spot-on products available include those containing fipronil, imidicloprid, methoprene, and permethrin. Currently, over 15 brands of permethrin spot-on products are labelled for use in dogs only. These products contain high concentrations (45-65%) of permethrin insecticide and are becoming a very popular choice for flea and tick control for dogs. Cats are highly sensitive to permethrin and inappropriate or accidental application of these products could be fatal. Though they have a wide margin of safety when used appropriately on dogs, even small amounts of permethrin spot-on products can cause severe clinical signs in cats. Indications of this species sensitivity have been documented by the National Animal Poison Control Centre (NAPCC). In most cases, the owner applied the concentrated permethrin-containing product to cats accidentally or intentionally. In some situations, the exposure seems to have resulted when the product was used on the dog and cats were playing with the dog.
Roder, J. D. (2001). <u>Veterinary toxicology</u> . Boston, Butterworth Heinemann.	2001	USA	Pyrethroids and pyrethrins (pages 251-254) No mention of especial sensitivity of cats to permethrin or SPs
Sutton, N. M. and A. Campbell (2008). "The effect of publicity on the frequency of feline permethrin exposures reported to the Veterinary Poisons Information Service, London." <u>Clinical Toxicology</u> 46 (5): 385-385.	2008	UK	
Sutton, N. M., N. Bates, et al. (2007). "Clinical effects and outcome of feline permethrin spot-on poisonings reported to the Veterinary Poisons Information Service (VPIS), London." <u>Journal of Feline Medicine and Surgery</u> 9 (4): 335-339.	2007	UK	Permethrin is a pyrethroid insecticide used in dermally applied spot-on flea treatments for dogs. Permethrin-based spot-on preparations are contraindicated in cats because of the high risk of toxicosis. The Veterinary Poisons Information Service (VPIS) is a 24-h access telephone service that provides veterinary professionals in the United Kingdom with information on the management of poisoned animals. In a review of 286 cases reported to the VPIS regarding inappropriate feline exposure to permethrin spot-on (PSO) preparations, 96.9% were symptomatic. Increased muscular activity (as evidenced by twitching, tremor, muscle fasciculations or convulsions) was common and occurred in 87.8% of cases. The duration of increased muscle activity was long, with convulsions lasting on average 38.9 h and tremors 32 h. Recovery typically occurred within 2 to 3 days but in some cases took 5 to 7 days. Death occurred in 10.5% of cases. http://www.fabcats.org/esfm/permethrin.pdf
Sutton, N., N. Bates, et al. (2007). "Seasonal rise in	2007	UK	SIR, – The Veterinary Poisons Information Service (VPIS) wishes to warn colleagues of

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
permethrin 'spot-on' poisoning in cats." <u>Veterinary Record</u> . 161 (7): 244-.			<p>an expected seasonal increase in feline exposures to permethrin 'spot-on' (PSO) preparations. In previous years, PSO inquiries have dramatically increased from June and July, and peaked between August and October. This period of high incidence reflects an increase in flea infestations, which fluctuate with temperature. Between June and July of this year, the VPIS has already noted a twofold increase in PSO inquiries, and anticipates a significant increase over the next few months. The VPIS suggests that permethrin poisoning be considered in the differential diagnosis for cats with unexplained tremor, twitching or convulsions. Effects of PSO poisoning usually occur rapidly, but can be delayed up to 72 hours. Delayed effects may prevent owners from associating PSO application with development of clinical effects. Furthermore, many owners are unaware that permethrin-treated dogs, and/or areas where treated dogs have been, can also be a source of feline contamination. Owners need to be questioned carefully about recent use of both feline and canine flea treatments. Where no clear history is available suspected cats should be thoroughly checked for evidence of recent 'spot-on' application. Despite warnings on product packaging, incidences of feline PSO exposure remain high. Since January 2007, the VPIS has recorded over 75 cases of feline PSO poisoning, with 135 cases in 2006. In many instances PSO poisoning was suspected but not confirmed. Not all practices call the VPIS for advice, especially where commonly encountered poisons are concerned. Consequently, the true incidence of feline PSO exposure is underestimated. The seriousness of feline permethrin poisoning is often misjudged. In a recent review of 286 VPIS cases, 87•8 per cent of cats developed increased muscular activity (tremor, twitching or convulsions), and 10•5 per cent died or were euthanased (Sutton and others 2007). Exposed cats should be treated immediately; our data suggest that decontamination of the fur is an undervalued intervention. Exposed cats should be washed promptly with lukewarm water and a mild detergent. Hot water should be avoided as it may increase dermal perfusion, while cold water may exacerbate toxicity. Convulsions or increased muscular activity should be managed conventionally. The effects may last several days. In severe cases benzodiazepines often prove ineffective and barbiturates or full anaesthesia may be required. In an effort to prevent poisoning from these products, cat owners should be encouraged to seek the advice of their veterinarian on appropriate methods of treating fleas. Nick Sutton, Nicola Bates, Alexander Campbell, VPIS, Medical Toxicology Unit, Avonley Road, London SE14 5ER</p>
Talcott, P. A. and D. C. Dorman (1997). "Pesticide exposures in companion animals." <u>Veterinary Medicine</u> 92 (2): 167-&.	1997	USA	Brief summary of pyrethrin and pyrethroid intoxication. No mention that cat may be particularly sensitive. Concluded that "the overall prognosis is very favourable, and most animals recover 24 to 72 hours after exposure."
Tjalve, H. (2004). "Adverse reactions to veterinary drugs reported in Sweden during 2003, part 3."	2004	Sweden	During 2003, a total of 44 reports have been received for cats. There are few reports of deaths in cats, which have been given permethrin (Exspot vet spot-on) by their owners.

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
<u>Svensk Veterinartidning</u> 56 (15): 21-25.			This drug, which is a pyrethroid insecticide, is registered for dogs.
Tjalve, H. (2008). "Adverse reactions in cats and reactions in humans to veterinary drugs reported in Sweden during 2005 and 2006." <u>Svensk Veterinartidning</u> 60 (1): 19-25.	2008	Sweden	The present article describes adverse reactions in cats and adverse reactions in humans to drugs registered for use in animals reported by Swedish veterinarians during 2005 and 2006. There were several reports of serious intoxications (including deaths) in cats, which were given permethrin (Exspot(R) vet spot-on) by the animal owners. This drug, which is a pyrethroid insecticide, is only registered for dogs. There were two reports of humans who experienced rather mild negative reactions after that their dogs had been treated with permethrin.
Tjalve, H. (2009). "Adverse reactions to veterinary medicinal products: an overview based on the Swedish experience." <u>Journal of Veterinary Pharmacology and Therapeutics</u> 32 (s1): 41-44.	2009	Sweden	PERMETHRIN (PSO) CATS Examples of other drugs which have been reported to cause negative effects in cats are antibiotics, antiparasitic agents and NSAID. There are several reports of serious intoxications, including deaths, in cats which by the animal owners were given a spot-on permethrin-preparation registered for dogs. This substance is degraded by glucuronide transferase. It is possible that the sensitivity of cats to permethrin is related to the fact that the feline liver is deficient in this enzyme.
Trammel, H. L. and W. B. Buck (1990). <u>Tenth Annual Report of the Illinois Animal Poison Information Center</u> , Kendall Hunt Pub Co.	1990	USA	[Referred to by Hansen et al 1994: "Data published by the National Animal Poison Control Center (NAPCC) provide an overview of the incidence of toxicosis to pyrethrin and pyrethroid insecticidal products reported by animal owners and veterinarians with regard to adverse reactions in dogs, cats, and other species." In 1988: "There were 62 cases involving cats and 23 cases involving dogs with regard to the pyrethroid permethrin. Permethrin cases were assessed as a toxicosis or a suspected toxicosis in 76% (n=47) of the cases involving cats compared with 22% (n=5) for dogs."]
Valentine, W. M. (1990). "Pyrethrin and pyrethroid insecticides." <u>Veterinary Clinics of North America: Small Animal Practice</u> 20 (2): 375-382.	1990	USA	Pyrethroids have a wide spectrum of insecticidal potency, vertebrate toxicity, and environmental stability. The exceptionally high selectivity ratios of pyrethrins and pyrethroids have resulted in their use for insect control in numerous formulations. A primary effect of pyrethroids is to slow the closing of the sodium activation gate in nerve cells. All pyrethroids have essentially the same basic mechanism of action on voltage-dependent sodium channels but differ in the magnitude of effect. Based on clinical signs, electrophysiologic responses, and chemical structure, pyrethroids can be classified as Type I or Type II. Inhibition of the GABAA receptor appears to be an additional mechanism of Type II pyrethroids. Clinical signs in small animals during a pyrethroid toxicosis vary but are generally attributable to neural dysfunction. Treatment consists of decontamination procedures and application of appropriate symptomatic care, including control of seizures if necessary (methocarbamol, diazepam, phenobarbital, pentobarbital). Cat not identified as especially sensitive to pyrethroids. Cat mentioned in relationship to intoxication with a product containing both fenvalerate and DEET.
Valentine, W. M. and V. R. Beasley (1989). Pyrethrins and pyrethroids. <u>Current Veterinary</u>	1989	USA	No mention that cat may be especially sensitive to SPs. "There have been few studies on the toxicity of pyrethrins and pyrethroids to domestic animals." Review

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
Therapy X Small Animal Practice. J. D. Bonagura. Philadelphia, W. B. Saunders Company: 137-140.			provides summary of mode of action, pyrethroid toxicity syndromes (type I and II), ion channel effects, GABA and cGMP effects, clinical signs, diagnosis and treatment.
Volmer, P. A. (2004). Pyrethrins and pyrethroids. <u>Clinical veterinary toxicology</u> . K. H. Plumlee. St. Louis, Mo. :, Mosby: 188-192.	2004	USA	Spot-on permethrin (45-65%) flea products for dogs are available over-the-counter and are extremely toxic to cats. "Cats exposed to a permethrin spot-on intended for canines should be treated as medical emergencies because of their profound sensitivity to these products." "Cats exposed to a concentrated permethrin-containing product may have a guarded prognosis if treatment is delayed and severe signs have already developed."
Volmer, P. A., S. A. Kahn, et al. (1998). "Warning against use of some permethrin products in cats." <u>Journal of the American Veterinary Medical Association</u> 213 (6): 800-1.	1998	USA	Letter. "When permethrin-containing "spot-on" products are used on dogs, as directed by the label, adverse reactions are uncommon. Unfortunately, many pet owners do not follow label directions or warnings and apply the products in an off-label manner to cats. The inappropriate application of dog-only permethrin-containing "spot-on" formulations on cats results in severe toxicosis."
Volmer, P. A., S. A. Khan, et al. (1998). "Permethrin spot-on products can be toxic in cats." <u>Veterinary Medicine</u> 93 : 1039.	1998	USA	
Walker, F. S. (2002). "Seizure-like behavior in cats." <u>Can Vet J</u> 43 (1): 3.	2002	Canada	When considering "rule outs" for severe seizure-like behavior in cats, clinicians should consider exposure to the over-the-counter topical flea product Zodiac Spot-On [etofenprox + S-methoprene?]. Our clinic has encountered 2 cases of cats having seizures after exposure to the product. In October 2000, a cat presented after rubbing up against a dog that had just been treated with Zodiac. Just recently, we had a cat that presented with similar symptoms after being treated with the feline product 2 days before. He had also been treated in the previous 2 months without incident. The drugs normally used to control seizures (valium, phenobarbital) do not work in this situation. The treatment that we have found to be effective is methocarbamol (Robaxin, 500 mg; Whitehall-Robins, Mississauga, Ontario), 75-100 mg/kg bodyweight (BW), dissolved and administered in a saline enema, and then repeated 20-30 min later at 1/3 to 1/2 of the original dose. The maximum dose is 300 mg/kg BW/d. The treatment can be repeated on subsequent days.
Whittem, T. (1995). "Pyrethrin and pyrethroid insecticide intoxication in cats." <u>Compendium on Continuing Education for the Practicing Veterinarian</u> 17 (4): 489...495.	1995	New Zealand	Review of mechanisms of action and toxicity, ADME, clinical signs, diagnosis and treatment. Cats appear more frequently intoxicated than other domesticated species. "Recommendations for use of pyrethrins and pyrethroids must be made after careful consideration of the formulation of the particular product, the age and health of the patient, and the likelihood that appropriate dosing regimens are followed by the owner."
Whittem, T. and J. M. Katz (1991). "Pyrethrin and pyrethroid insecticide toxicity in cats: a retrospective case study." <u>Proceedings of the 9th Annual Veterinary Medicine Forum of the American College</u>	1991	USA	Pyrethrins and their synthetic analogues, pyrethroids (PYs), are the most commonly used insecticides for the treatment of ectoparasite infestation in cats. A retrospective study of the cases of clinical PY toxicity in cats reported to the GAPIC [Georgia Animal Poison Information Center] in 1989 and 1990 was undertaken to identify relationships

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
of Veterinary Internal Medicine: 890.			<p>between clinical signs, rate of onset of signs, and formulations. Of 1360 reports of exposure of cats to hazardous materials, 520 (38%) involved insecticides of which 116 (22%) were PY exposures. Of reports of PY exposure, 87 (75%) showed clinical signs including central and peripheral neuropathies (69 & 27.5%), respiratory distress (18.4%), vomiting and other gastro-intestinal signs (14.9 & 8%), anorexia (13.8%), cardio-vascular abnormalities (4.6%), and death (3.4%). Dermal application was the primary route in 94% cases. Although PY classes are defined by an α-cyano moiety which reportedly increases toxicity, analysis by χ^2 test for independence revealed no correlations between rate of onset, severity, or type of clinical signs and the class of PY. Inclusion of cytochrome P450 inhibitors had no effects on examined parameters. Inclusions of hydrocarbons in formulations were correlated with occurrence of cardiac signs ($p=0.02$) whereas alcohol formulations were correlated with occurrence of peripheral neuropathies ($p=0.01$). The rate of onset of toxicity is rapid with 42% cases symptomatic in less than one hour.</p>
<p>Wisner, T. (2001). "Small Animal Toxicoses - Insecticides." Retrieved 24 August, 2009, from http://www.vspn.org/Library/misc/VSPN_M01289.htm</p>	2001	USA	<p>Permethrin is approved for small animal flea control, large animal topical fly control, crops, ornamental plants and human use. Permethrin is found in shampoos, dips, foggers, spot-ons, and sprays for small animal use. Permethrin is a synthetic type I pyrethrin. Type I pyrethrins bind to the sodium channels on nerves and alter the voltage-dependent gating kinetics. This causes reversible prolongation of sodium conductance in the nerve axons and results in repetitive nerve discharges. (Valentine, 1990; Casida, 1983) This effect is enhanced in hypothermic mammals and in cold-blooded animals. Oral absorption of permethrin is rapid for all species, but dermal absorption of permethrin varies. Rat skin absorbs significantly more permethrin than monkey skin. (Sidon, 1988) Permethrin is highly lipid soluble and concentrates in nervous tissue at 1.5 - 7.5 times the plasma concentration. (Anadon, 1991) Permethrins are broken down in the liver and are excreted in the urine. (Tomlin, 1994). Permethrins appear to be relatively safe in dogs. Smaller dogs seem to have a greater risk of toxicity and any animal can have a dermal hypersensitivity reaction to a spot-on. These dermal hypersensitivity reactions may be to the active ingredient or to the carriers. Skin reactions can be treated with bathing +/- antihistamines or steroids. Cats are more likely than dogs to develop pyrethroid toxicosis. This is due to the feline liver being inefficient at glucuronide conjugation. Glucuronide conjugation is needed to metabolize permethrin. The low concentration products approved for cats contain 0.05-0.1% of permethrin and do not seem to cause the signs that the concentrated (45-65% permethrin) canine spot-ons do. (MacDonald, 1995) Permethrin toxicity usually occurs when the owner applies the dog spot-on product to the cat; however, cats which actively groom or engage in close physical contact with recently treated dogs may also be at risk of toxic exposure. The severity of permethrin toxicity</p>

CITATION	YEAR	COUNTRY of AUTHOR	NOTES
			<p>varies with each individual. Some cats develop signs when only "one drop" is applied, while others show no clinical signs after an entire vial is used. Onset of clinical signs is usually within a few hours of exposure but may be delayed up to 24 hours. The most common clinical signs of permethrin toxicity in cats are muscle tremors and seizures. Hypersalivation, depression, vomiting, anorexia and even death may also be seen. Methocarbamol (50-150mg/kg IV bolus, titrate up as needed, but do not exceed 330mg/kg/d) works best to control the tremors. If no injectable methocarbamol is available, the oral form may be dissolved in water and given rectally. If the cat is actively seizing, barbiturates, propofol or inhalant anesthesia can be used. Valium does not seem to work as well to control permethrin induced tremors and seizures. Once stabilized, a bath with liquid dish washing detergent should be given. Permethrins appear to have no direct action on the liver or kidneys, but fluids may be needed to help protect kidneys from myoglobin break-down products in actively trembling cats. Prognosis for mildly trembling cats is usually good, but treatment may last 24-48 hours. Uncontrollable seizures or extended duration of seizure activity despite aggressive treatment efforts worsens the prognosis. For definitive confirmation of permethrin toxicosis, urine and plasma can be analyzed for permethrin using liquid chromatography. (Anadon, 1991; Sidon, 1991) Although not a routine analysis, necropsy samples of liver, fat, brain, and/or CSF fluid can also be used to confirm exposure.</p>
Woo, A. and P. Lunn (2004). "Permethrin toxicity in cats." <u>Australian Veterinary Practitioner</u> 34 (4): 148-151.	2004	Australia	This report details information on toxicity in cats following application with permethrin-containing ectoparasitocides indicated for dogs, or contact with permethrin-treated dogs. The case study demonstrates the potential for cats to develop permethrin toxicity following inadvertent application of a permethrin-containing product by a pet owner.
Woodward, K. N. (2005). "Veterinary pharmacovigilance. Part 2. Veterinary pharmacovigilance in practice - the operation of a spontaneous reporting scheme in a European Union country - the UK, and schemes in other countries." <u>Journal of Veterinary Pharmacology and Therapeutics</u> 28 (2): 149-170.	2005	UK	Permethrin (page 153-154) "The potential toxicity of permethrin in the cat ... has also been publicized."
Woodward, K. N. (2005). "Veterinary pharmacovigilance. Part 3. Adverse effects of veterinary medicinal products in animals and on the environment." <u>Journal of Veterinary Pharmacology and Therapeutics</u> 28 (2): 171-184.	2005	UK	Permethrin (page 171) Cats are also more susceptible to the toxic effects of permethrin because unlike some other mammalian species they lack the necessary detoxification pathways (Volmer et al., 1998; Meyer, 1999; Gray, 2001; Martin & Campbell, 2000; Richardson, 2000).