Pyrethrin Toxicity in Cats

By Alison Allukian, DVM

angell.org/emergency

emergency@angell.org

617-522-7282

March 2023

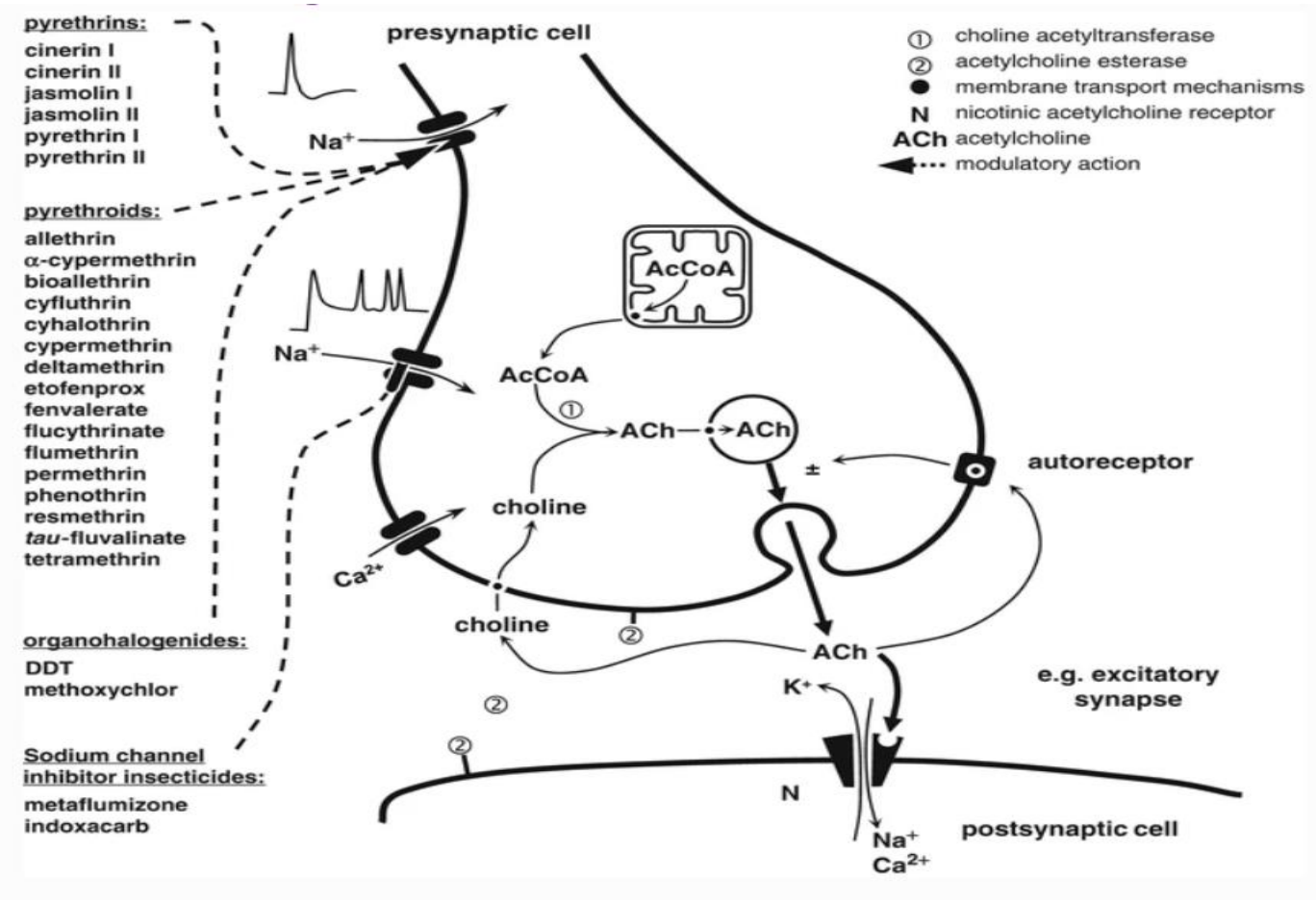
Introduction

Pyrethrin toxicity in cats commonly occurs during warmer months when flea and tick control products are applied topically. The clinical signs of pyrethrin toxicity are neuroexcitation and can range from mild to severe. In the most severe cases of pyrethrin toxicity, it results from topical flea treatment applied to cats when it is only labeled for use in dogs. This is due to the higher concentration of pyrethroid found in dog topical flea treatment. Pyrethrins are an insecticide derived from chrysanthemum flowers (*Chrysanthemum cinerariifolium and C. cineum*). At the same time, pyrethroids are their synthetic derivatives, are more stable and potent, and are particularly found in spot-on treatments. There are other formulations other than spot on, such as dips, sprays, powders, shampoos, gels, collars, and aerosol bombs, that can cause the same toxicity.

Metabolism and Mechanism of Toxicity

Cats are more susceptible than dogs to pyrethrin toxicity because their liver is inefficient at glucuronide conjugation. Glucuronide conjugation is a metabolic pathway in which drugs are combined with glucuronic acid to form more water-soluble compounds, making them more readily excreted in urine or bile. Pyrethrins and pyrethroids are hydrolyzed by tissue and plasma esterases and then oxidized by hepatic mixed function oxidases. All metabolites (glycine, glucuronides, glucosides, sulfates) are inactive and are renally excreted after hydroxylation or conjugation.[1] Since the feline liver is inefficient at glucuronide conjugation, there is an accumulation of phase I metabolites which are also the most potent. Phase I metabolites decelerate detoxification by slowing down the breakdown of the parent compound.[2]

Pyrethrin's neurotoxic effects are exerted on the central and peripheral nervous system via the voltage-sensitive sodium channels. It binds to the voltage-gated sodium channels of myelinated nerves, slowing their closure (inactivation) and resulting in repetitive neuronal discharge.[2,3] There is also evidence that pyrethroids may interact with calcium and chloride voltage-dependent channels, further contributing to its neurotoxic Mechanism of action (see the below diagram).



Pyrethrins/pyrethroids affect neural transmission by slowing the inactivation of the voltage-gated sodium channels.[4]

Diagnosis and Clinical Signs

Diagnosis is typically based on the history of recent exposure, clinical signs, and exclusion of other causes that can cause similar clinical signs. If there is no history of exposure, then other tremor-inducing toxins should be considered. It is possible to screen for pyrethrins/pyrethroids in blood and tissue levels, but since there are no established LD50 values for dogs and cats, their presence only indicates exposure.[2]

The most common clinical signs are twitching, tremors, hypersalivation, mydriasis, and seizures. Clinical signs can appear within a few minutes to hours but may take as long as 72 hours. Signs can range from mild to severe. In the mild to moderate affected group, signs may be hypersalivation, mild tremors, depression, hyperexcitability, or GI signs. Some cats may roll on their back and rub it due to paresthesia. In the more severely affected group, cats may appear disoriented, hyperthermic and have muscle fasciculations, generalized tremors, or seizures.

Treatment and Prognosis

There is no antidote for pyrethrin toxicity, and treatment is aimed at decontamination and managing clinical signs.

In animals with topical exposure, a warm bath with a mild soap detergent will help remove the lipophilic toxin**.** Lukewarm water is recommended to avoid increased absorption from increased blood flow with a warm bath or exacerbated tremors from hypothermia with low bath temperatures. Hyperthermia can occur secondary to the tremoring, but it is usually self-limiting once the tremoring/seizures are controlled, and intravenous fluids have been administered. Hypothermia should be avoided as this can increase the pyrethrin toxicity by exacerbating the tremors and prolonging recovery. If there is any oral ingestion, then general guidelines for GI decontamination apply.

Methocarbamol is administered as a first line of therapy for muscle tremors. It is a muscle relaxant with a mechanism of action in the CNS. Due to this, methocarbamol can exacerbate CNS sedation, mainly when used with additional drugs such as diazepam and barbiturates. Frequently, these other drugs may be needed as methocarbamol does not entirely stop the muscle tremors. In severely affected cats with ongoing tremoring, lipid therapy can be useful. One study saw a faster resolution of clinical signs when administering lipid therapy than a placebo.[3] In another small study of three cats, intravenous lipid emulsion therapy resulted in decreased hospitalization stay and marked clinical improvement of muscle tremors, and there were minimal side effects.[5]

In general, the prognosis for pyrethrin toxicity is excellent as long as appropriate medical intervention is performed. Cats are typically well enough to be discharged within 24-96 hours from presentation unless there is systemic illness or brain injury. Without treatment, fatal outcomes are possible with highly concentrated pyrethroids.

References

1. Soderlund DM, Clark JM, Sheets LP, et al.: Mechanisms of pyrethroid neurotoxicity: Implications for cumulative risk assessment, *Toxicology* 171:3, 2002
2. Pyrethrins. Boller M and Silverstein DC. Chapter 94: Pyrethrins in Small Animal Critical Care Medicine.
3. Peacock R., Hosgood G., Swindells K., Smart L. A randomized, controlled clinical trial of intravenous lipid emulsion as adjunctive treatment for permethrin toxicosis in cats. *JVECC* 2015 Sept-Oct: 25 (5): 597-605.
4. Turber, A. (2015). Ectoparasiticides: Blockers/Modulators of Voltage-Gated Sodium Channels. In: Melhorn, H. (eds) Encyclopedia of Parasitology. Springer, Berlin, Heidelberg.
5. Haworth MD, Smart L. Use of intravenous lipid therapy in three cases of feline permethrin toxicosis. *JVECC* 22:697-702, 2012.