

DRAGONFLY HOLISTIC
VETERINARY CARE

IDENTIFYING ADVERSE REACTIONS TO ANTIPARASITIC PESTICIDES

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What Every Pet Parent Should Know - Adverse Effects of Antiparasitic Pesticides

ONE OF THE MOST COMMON QUESTIONS I GET ASKED IS:

"What is the safest parasite prevention for my pet?"

UNFORTUNATELY, THERE ISN'T A SIMPLE ANSWER.

Insects and parasites such as; mosquitoes, ticks, flies, fleas and bees can transmit diseases, but at the same time some of the products marketed as antiparasitic preventatives can also be associated with risk of severe adverse events (side effects). As a pet owner or pet care professional, you must be able to make a balanced decision on 'risk to benefit' of the products that are available. Understanding these products and how to identify a potential adverse reaction will help keep pets healthy.

There are two types of parasites to combat;

- Internal Parasites (Endo-parasites); hookworms, tapeworms, whipworms, heartworms, etc.
- External Parasites (Ecto-parasites); mosquitoes, ticks, flies, fleas, bees

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Below is a list of products offered for management of parasites.

ORAL PRODUCTS:

Typically, these products are in pill form for internal consumption.

Oral pharmaceutical products (pills/chewables) in the 'isoxazoline' class:

- Simparica® (sarolaner)
- Simparica Trio® (sarolaner, moxidectin, pyrantel)
- NexGard® (afoxolaner)
- Bravecto® (topical also available; fluralaner)
- Credelio® (lotilaner)
- Revolution Plus® for cats (a topical product; selamectin and sarolaner)

These products are designed to work by disrupting the CNS central nervous system of their targets. These 'isoxazolines' are metabolized by your pets' organs and then absorbed into the blood stream of your pet and are transferred to the parasite when it bites them, as an attempt to lead to the death of the parasite within hours to days. These products do not prevent a bite or treat a disease; they are designed to kill the parasite after it bites the animal.

In 2018 The U.S. Food and Drug Administration (USDA) alerted pet owners and veterinarians to be aware of the potential for neurologic adverse events in dogs and cats when treated with drugs that are in the isoxazoline class. The FDA and the manufacturers of the 'isoxazoline based' products have also issued warnings of adverse events associated with the use of this class of product.

Evidence indicates that isoxazolines can cross the blood-brain barrier (BBB), and neurological adverse effects have been reported in susceptible animals2. Researchers have specifically noted that reducing brain exposure may reduce neurological side effects.

If you choose to use a different modality, let your veterinarian know so that they can suggest alternatives.

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TOPICAL PRODUCTS :

Topical products may be used in lieu of 'internal' products, thus providing a potentially safer form of treatment, These products are typically spot-ons.

Here is a list of pharmaceutical topical spot-on products designed to repel and/or kill parasites when they bite your pet:

- Frontline Plus®
- Advantix® and Advantix II®
- Vectra 3D®
- Trifexis®
- Frontline Shield®

The topicals, except for the isoxazolines Bravecto topical and Revolution Plus, are intended to stay more external. They are applied to your pet's back and spread through your pet's skin oils, and are passed to the tick/bug from that more external position when it bites. This mechanism isn't perfect, though. Some amount of drug can still pass through the skin into your pet's body, which is why some pets will get sick even from these. But in general, it tends to be to a lesser extent than the oral isoxazolines drugs.

Here is a list of 'Essential Oil Topicals' (sprays and spot on's) designed to repel parasites:

- AnimalEO.info essential oil blends (Away, Evict, Oust)
- Skout's Honor
- Kin-Kind
- Wondercide
- Only Natural Pet
- Tropiclean
- Vets Best
- Sunday

These essential oil topicals provide an alternative safer solution to consider. These are typically applied to the pets' legs, sides, and belly. These essential oils are designed to deter and prevent parasites from hopping onto the pet or biting the skin. Instructions are generally included with the product.

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Heartworm Prevention:

Heartworm disease is unique because it begins with an external (ecto) parasite, a mosquito, but then develops into an internal (endo) parasite, the heartworm. Heartworms are transmitted when a dog is bitten by an infected mosquito carrying heartworm larvae. Once inside the dog, the larvae migrate through the tissues and bloodstream, eventually developing into adult worms that live in the heart, lungs, and associated blood vessels.



Mosquito activity generally increases during warmer weather above 50 degrees, although heartworm transmission can occur whenever mosquitoes are active.

Common heartworm preventives include ivermectin- and moxidectin-based products. Some dogs with the MDR1 gene mutation (commonly seen in breeds such as Collies, Australian Shepherds, and related breeds) may have increased sensitivity to certain medications, so prevention choices should be discussed with a veterinarian. I recommend DNA testing your pet at home to screen for this mutation, as it can also affect how their body handles other medications. Many at-home DNA tests are available today, such as the Embark DNA test. Some owners work with their veterinarians to develop customized heartworm prevention plans, such as compounding for your specific dog, but any changes to standard heartworm prevention should be made under veterinary guidance.

Regardless of the prevention product used, reducing mosquito exposure is beneficial because mosquitoes can transmit other diseases as well. Topical repellents and other mosquito-control measures may help reduce mosquito bites.

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Here is a list of pharmaceutical heartworm prevention products designed to kill heartworm larvae before they mature into a heartworm:

- Interceptor or Interceptor Plus (milbemycin or milbemycin + praziquantel dewormer)
- Custom formulated Ivermectin or Moxidectin (usually put on top of food)
- Sentinel (Interceptor + mild flea control)
- Tri-heart or Triheart Plus (Ivermectin or Ivermectin + pyrantel dewormer)
- Heartguard Plus (Ivermectin + pyrantel dewormer)
- Simparica Trio, Credelio Quatro, Nexgard Plus - all contain an isoxazaline for flea/tick control + a heartworm medicine like moxidectin +/- pyrantel dewormer)

Some pet owners choose heartworm prevention alone, and address other intestinal worms as needed through parasite testing at the frequency recommended by their veterinarian.

What is the BBB?

A recent study suggests that some pharmaceutical parasite prevention substances may pass through a pet's **blood-brain barrier** and reach the brain-2. Mammals have a protective system called the Blood-Brain Barrier (BBB). Think of the BBB as your pet's brain armor. It is a specialized lining between the bloodstream and the brain that prevents many medications, toxins, and infectious organisms from entering the brain and spine nerve tissue. The **blood-brain barrier (BBB)** plays a crucial role in protecting the brain from substances circulating in the bloodstream. When certain drugs, toxins, infections, inflammatory processes, or diseases affect the BBB, substances that normally would be restricted can gain greater access to brain tissue and potentially contribute to neurological symptoms. Sometimes these symptoms can be easy to identify and other times it is more difficult.

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The traditional assumption has been that these antiparasitic products remain outside the brain, where they can affect parasites without affecting the pet. However, years of experience with these drugs and emerging research suggests the situation is more complicated. Having a keen eye on how to identify more of the common symptoms is helpful for making a proper association.

Permeability of the BBB:

Research in aging dogs has shown that many senior dogs develop changes within the brain, including cerebral amyloid angiopathy (CAA) and microscopic hemorrhages (very small bleeds). These changes may weaken the blood-brain barrier in older patients, particularly those over 7 years old. In one of his very informative Facebook posts from May 2025, integrative veterinary neurologist Dr. Curtis Dewey notes that studies have found evidence of CAA in approximately 70% of dogs over 8-10 years of age, even when those dogs showed no obvious neurological symptoms. If blood vessels within the brain are damaged or leaky, it becomes difficult to assume the blood-brain barrier remains fully intact.

<u>This raises an important question</u>:
If the blood-brain barrier becomes more permeable with age or disease, could more of these compounds (and others) gain access to the nervous system? We don't know for sure yet, but it is a question very worth considering, especially in senior pets.[6-14]



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Axonal Transport:

A recently published review proposed another possible mechanism.[2]

Certain parasite-control compounds are highly fat-soluble (lipophilic). Researchers suggest they may be capable of entering nerve endings in the body and being transported back toward the brain through a process called axonal transport. This mechanism hijacks the nerve cell's normal intracellular transport system, giving whatever hitches a ride a highway straight to the brain. This is already known to happen with a few infectious diseases (e.g. Rabies, herpes) and toxins (tetanus, heavy metals, organophosphate pesticides, chemotherapy drugs).

In other words, even if the blood-brain barrier remains intact, there may be other pathways that allow these compounds to reach nervous tissue. More research is needed to know if our commonly used pet parasite preventatives utilize this mechanism, but it is an active area of investigation.

What About PFAS?

Another emerging concern involves PFAS (per- and polyfluoroalkyl substances), often referred to as "forever chemicals." PFAS are found throughout our environment and have been associated with neurological side effects. They are commonly found in plastics, such as those in which our conventional parasite preventatives are stored. Additionally, the final 2025 report from the Minnesota Department of Agriculture (MDA) revealed that under the state's broad, structure-based definition, the active ingredients of 97 pesticides registered for use are **themselves** classified as PFAS.

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Research suggests PFAS can:

- Cross AND damage the blood-brain barrier
- Increase oxidative stress within nerve tissue, effectively making it more vulnerable
- Alter nervous system communication chemicals like glutamate and dopamine
- Disrupt calcium regulation within cells
- Increase nervous system inflammation

Some researchers have also raised concerns that PFAS-related changes to the blood-brain barrier could increase the brain's vulnerability to other neurotoxic compounds. Again, this is an evolving area of science, but it highlights how complex neurological risk assessment can be. [2-5]



Are Puppies and Kittens More Vulnerable?

Potentially. The developing nervous system is generally more sensitive to toxic exposures than the mature nervous system. Their BBB is not yet fully developed, which suggests that increased "leakiness" and, therefore, sensitivity to drugs and toxins is likely. Their brains and nerves are also growing, connecting, and refining rapidly during their growth period. This may also translate into increased sensitivity to drugs and toxins. Research in both humans and animals has identified critical developmental periods during which neurotoxic exposures may have more significant long-term effects.15 Additionally, their detoxification pathways are still maturing, which can mean slower clearance of and longer exposure to drugs and toxins. Risk-benefit decisions should be made thoughtfully.

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Potential Adverse Effects of Parasiticides:

In June of 2020, Project Jake found that 67% of pets who received a parasiticide drug had noticeable side effects. Manufacturers safety sheets and studies have mentioned these reported side effects include:

Gastrointestinal

- Vomiting
- Diarrhea
- Decreased appetite

General Lethargy

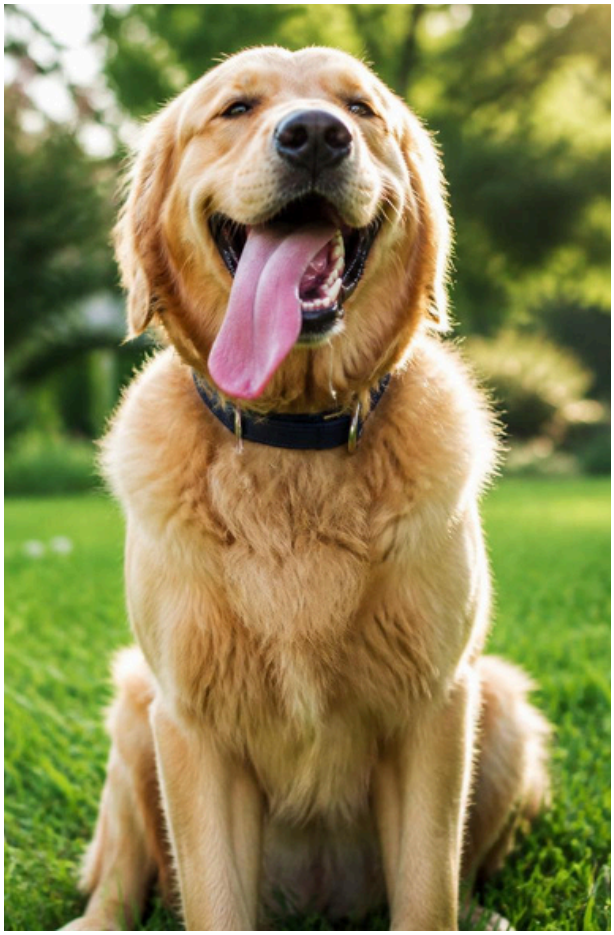
- Decreased energy
- Behavioral changes
- Increased drinking
- Skin itching, flaking
- Paws, chewing paws, red paws

Neurological

- Tremors, Shaky legs
- Muscle twitching
- Drooling, increased salivation
- Loss of coordination (ataxia)
- Seizures
- Visionary changes, loss, sensitive to light
- Behavioral changes (anxiety, aggression, clinginess)
- Cognitive changes (disorientation, confusion, sleep disturbances, mood changes)

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WHY DOES MY DOG DROOL?



Drooling, involuntary dripping, or increased salivation can result from dental disease, oral pain, or an unpleasant taste. However, involuntary drooling may also signal a neurological adverse event, especially if it appears during excitement or activity, such as exercise. If you notice this in your dog, review the products your dog is taking and check whether any are associated with neurological adverse reactions. This symptom may indicate that a neurotoxic substance has reached the brain through a more permeable blood-brain barrier.

WHAT TO DO IF I NOTICE MY PET MIGHT BE HAVING AN ADVERSE REACTION:

If you feel your pet is having an adverse reaction to a medication, it is best to seek medical attention to investigate the cause and formulate an appropriate treatment plan. A holistic veterinarian can be a great resource for identifying the cause of unusual symptoms, rather than simply treating the symptom itself. Switching products or discontinuing use of a product can provide your pet with relief over time.

Check the safety sheet of any products you are giving your pet. Many of the symptoms listed above are also listed on the safety sheets of the products.

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- You can report potential adverse events from most flea/tick preventatives to the USDA: https://www.aphis.usda.gov/veterinary-biologics/adverse-event.

- If you would like to make a comment to the FDA on a product you can also do so at: https://www.regulations.gov/commenton/FDA-2026-P-6249-0001

MY APPROACH TO PARASITE PREVENTION:

I do not believe every pet needs the strongest product available. The Shih Tzu who uses a weewee pad and the Pointer who is out hunting in the woods are very different dogs, with very different parasite exposure risk. Instead, I recommend matching protection to the pet's actual location and exposure risk.

HIGH-RISK PETS:

For pets living in heavily wooded areas or regions with significant tick pressure, I generally recommend layering multiple strategies.

These may include:

- TiCK MiTT® wipe-downs after every outdoor adventure
- General grooming & inspection
- Tickless ultrasonic tags or FleasGone tags
- Essential oil repellents (e.g. Wondercide of AnimalEO brands)
- Baltic amber collars
- Buck Mountain Parasite Dust
- Environmental control measures – staying away from areas where insects thrive, wet areas
- Seasonal considerations- less protection is typically needed in the winter when tick levels are much lower

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When I need stronger protection, I generally prefer to start with the least toxic options likely to be effective, such as Frontline Plus or the other, stronger topical options listed in the beginning.

LOW-RISK PETS:

For pets with relatively low exposure, one or two natural approaches may be sufficient.

ENVIRONMENTAL CONTROL MATTERS:

One of the most overlooked aspects of parasite prevention is reducing environmental exposure.

Here are some pet friendly yard treatments to help manage insects safely:

- Wondercide®
- Sunday Nix Ticks spray
- Beneficial nematodes - we like Arbico Organics' products.
- Tick-deterring plants such as mints and calendula
- Fencing to reduce wildlife
- Chickens - they love to eat ticks!
- Clearing away leaf litter frequently - ticks love to hide and survive the winter under leaves
- Resolving any swampy or wet damp areas
- Keeping grassy areas properly maintained and clean play areas inside and out

Reducing the number of ticks in your pet's environment often reduces the need for stronger medications.

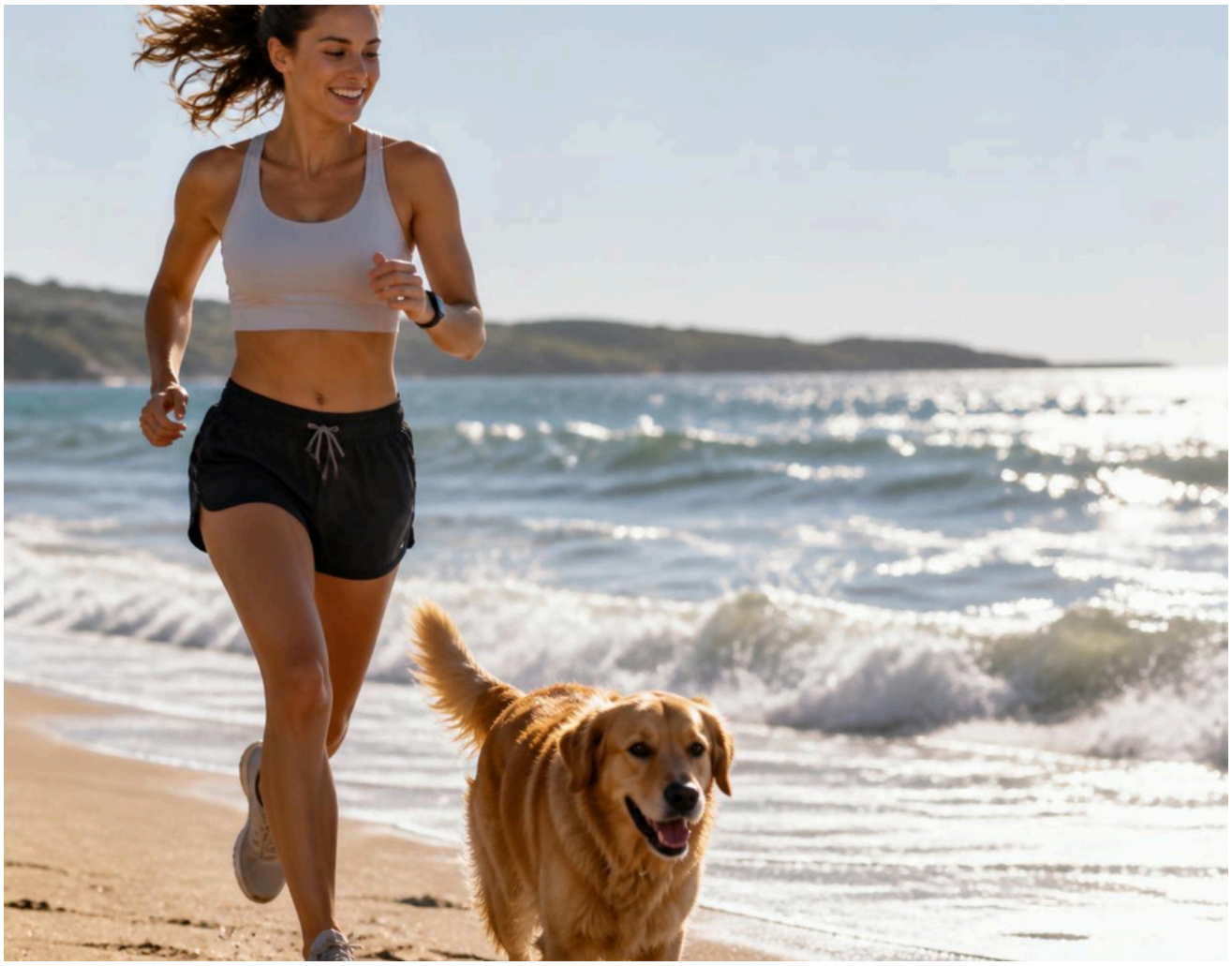
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THE BOTTOM LINE:

There is no perfectly safe parasite prevention. Every option carries risks and benefits.

For some pets, conventional medications may be appropriate. For others, a layered natural approach may provide adequate protection while reducing chemical exposure. My goal is to help pet owners make informed decisions based on their individual pet's age, health status, lifestyle, neurological history, level of parasite exposure and the pet owners' level of risk exposure.

As with most things in holistic medicine, the best answer is always "It Depends!"



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