

HEARTWORM DIAGNOSIS & TREATMENT

Heartworms have been diagnosed in all 50 states and in many places outside the U.S. Their most common hosts are dogs and other canids but cats, ferrets, sea lions and many other animals can get them as well. The scientific name of the heartworm parasite is *Dirofilaria Immitis* and these worms belong to the class of creatures called nematodes – as do roundworms and hookworms. They have a somewhat complicated life cycle, which is important to understand when you start thinking about prevention and treatment.

The life cycle of *D. immitis* is relatively long (6-9 months) compared with most parasitic nematodes. They are spread from dog to dog by mosquitoes, which become infected when taking a blood meal from a heartworm-infected host. The microfilaria taken up by the mosquito when it feeds are the first larval stage, called the L1 stage.

These larvae develop to their third stage inside the mosquito. Then they migrate through the body cavity of the insect to its head and mouthparts. The time required for the development of microfilariae to the infective stage in the mosquito is temperature-dependent. Development takes about 10-14 days. In cooler weather they are dormant or develop more slowly.

Infective, third-stage larvae (L3) are deposited in a droplet of hemolymph (mosquito blood) on the host while the mosquito is taking a blood meal. These L3 microfilariae enter the animal's body via the puncture wound in the skin made by the mosquito's mouthparts. Three days later most of the larvae are found in the subcutaneous tissues near their entry site. By day 21, most of the larvae have migrated to the abdominal tissues of the dog, and by day 41, they may be recovered from either the abdominal or thoracic tissues. They penetrate muscles and eventually veins, which transport them toward the heart and lungs. During this time they change from the L3 stage to L4.

L4 microfilaria molt to the final stage 50-70 days after the day the mosquito bit the host animal. Worms reach the blood vessels in the lungs as early as day 70 and all have arrived by day 120. The first worms entering the lungs on day 70-85 are 1-1.5 inches in length. When they are full-grown the female worms will be almost ten times larger than that. They become sexually mature about day 120 post infection, ready to start producing microfilariae of their own. These then are released into the circulation, where they stay until they are taken up by another mosquito. Dogs develop patent



infections (i.e., have next generation microfilaria circulating in their blood) as early as 6 months but usually by 7-9 months post-infection.

Cats are not the ideal host for heartworms and in cats most larvae do not survive to become adult worms in the heart. Cats usually have few, if any, adult worms living in the heart, whereas dogs can have dozens or even more than 100. Many larval worms die during their migration through the lungs in cats, so the symptoms of heartworm disease are mostly due to the damage that occurs within the lung tissue. Respiratory symptoms and vomiting are both common signs in cats, and, unfortunately, another sign is sudden death.

The most commonly used heartworm preventative drugs are the macrocyclic lactones (ivermectin, milbemycin oxime, moxidectin and selamectin). These drugs are very safe and possess anthelmintic activity against microfilaria, third- and fourth- stage larvae, and in some instances of continuous use, even young adult heartworms. All oral and topical macrocyclic lactone products are given monthly. The current recommendation of the American Heartworm Society is to give monthly preventative medication to all dogs all year long. This also protects against intestinal parasites more effectively and ensures if parasites do develop that the drug manufacturer will cover the pet's treatment on behalf of the client.

Lack of efficacy (LOE) of a heartworm preventive product is defined by the Center for Veterinary Medicine of the Food and Drug Administration (FDA) as "a dog testing heartworm positive while consistently receiving heartworm prevention." There are many possible reasons for LOE, including underdosing – giving a dose that is too small for the size of the pet, failure to administer the preventive at the appropriate time interval, failure of a dog to retain a dose (meaning he or she spit it back out or vomited it back up) and failure to absorb the active ingredient.

Annual blood testing for heartworms is an integral part of ensuring that prophylaxis is achieved and it ensures that more timely treatment can be provided to dogs that test positive so that damage to the heart and lungs is minimized. A dog should be tested prior to starting or changing products. Subsequent antigen testing should be performed annually thereafter, as recommended by AHS.

TREATMENT OF HEARTWORM DISEASE

Successfully treating heartworm disease in asymptomatic patients or those exhibiting signs of mild disease usually is straightforward, though it may occasionally become demanding if complications occur. Those with moderate or severe heartworm disease or patients with concurrent disease may be challenging. For example, we recently treated a heartworm-positive dog with moderate clinical signs, and she also had a tibial fracture requiring a bone plate and was nursing puppies. A long anesthetic procedure is worrisome whether you do it before or after administration of treatment and we had no idea whether melarsamine, the drug that we use to kill adult heartworms, would harm the puppies.

The goals of any heartworm treatment are to improve the clinical condition of the animal and to eliminate all life stages of the heartworms (microfilaria, larval stages, juveniles and adults) with minimal post-treatment complications.

Dogs exhibiting significant clinical signs of heartworm disease should be stabilized before administering an adulticide - a drug that kills adult heartworms. Testing before treatment should include CBC, chemistry panel, urinalysis and chest x-rays. We are looking for low platelet count, kidney damage and lung damage so that we can treat for any problems that have occurred secondary to the worms.

Many nematodes, including *D. immitis*, harbor gram-negative bacteria called *Wolbachia*. *Wolbachia* contribute to lung and kidney damage caused by heartworms. Heartworm positive dogs pretreated with ivermectin, which kills off microfilaria, and doxycycline, which kills the *Wolbachia* bacteria, prior to receiving melarsomine injections suffer less lung damage.

Melarsomine is not safe for use in cats but doxycycline and ivermectin would be expected to gradually decrease worm burdens in cats as they do in dogs. Supportive care is needed for clinical signs as for dogs.

Adult heartworms in dogs are killed by administration of melarsomine dihydrochloride, which is administered via deep intramuscular injection into the back muscles. This medication usually causes swelling and soreness at the injection site which may last for a few days. Ice packing and NSAID or tramadol administration can help to make the dog more comfortable for the first few days after the injections are administered.

The traditional standard two-injection melarsomine protocol, consisting of two injections 24 hours apart for treating class 1 and 2 heartworm disease (in which symptoms are absent or mild) is no longer recommended. This protocol kills about 90% of the adult worms. The alternate three-dose protocol, which is to give a single injection and then a month later two additional injections 24 hours apart is more effective, killing 98% of the worms. The current recommendation by AHS is to use the latter protocol for all classes. It's safer as well as more effective, because it initially kills fewer worms and the cumulative impact of worm emboli (pieces of dead heartworms washing into and becoming lodged in the lungs) on the diseased pulmonary arteries and lungs is reduced.

Pulmonary thromboembolism is an inevitable consequence of killing the adult heartworms and may be severe if infection is heavy and pulmonary arterial disease is extensive. If signs of embolism (low grade fever, coughing that may bring up blood, right heart failure) develop, they are usually evident within 7 to 10 days of melarsomine treatment, but may occur as late as four weeks afterwards. Mild embolism in relatively healthy areas of lung will cause no obvious symptoms.

Exercise restriction is critical during the critical month following the first injection and then again after the second/third injections. It's the most difficult part for the pet owner though. Younger, more active dogs are the most likely to have major problems from pulmonary embolism but are the most difficult to keep quiet.

The number of worms has an effect on the severity of disease, but of equal, if not greater, importance is the activity level of the dog. Controlled studies have shown that dogs infected by heartworms who were exercise-restricted took longer to develop clinical disease and developed less pulmonary vascular damage than dogs with smaller numbers of worms who were allowed moderate activity. Live heartworms can cause inflammation in the blood vessels but dying and dead heartworms cause a significant portion of the damage. As worms die from either natural causes or as a result of administration of adulticidal drugs, they decompose and small worm fragments lodge in the distal pulmonary arteriole and capillary beds in the caudal lung lobes, blocking blood flow. During exercise, the increased blood flow to these blocked vessels can cause capillaries to rupture and leads to scarring in the lungs. This can lead to right-sided heart failure.

Exercise restriction should be enforced from the time of heartworm diagnosis through the period of treatment and recovery, with the most extreme degree of exercise restriction recommended for the first four weeks following melarsomine administration.

For more detailed information and videos of the heartworm life cycle, visit www.heartwormsociety.org

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