

Diagnosis of Heartworm Disease

The chief issue in the diagnosis of heartworm disease centers around detecting heartworm infection. The following are a list of diagnostic methods that have been and are used in the detection of heartworms within the dog's body.

Because of the 5-month minimum migration time of the larval heartworm after infection, it is useless to test dogs younger than 5 months of age for heartworm. These puppies are too young to have adult heartworms and are too young to test positive under any circumstances.

Antigen Testing

Using genetic engineering, it has become possible to create extremely sensitive tests capable of detecting tiny pieces of adult heartworm skin circulating in the blood. In this way, very small numbers of adult worms can be detected - even single worm infections. This kind of testing has made it possible to detect infections in which no microfilariae are present: the so-called occult infections. Most of these immunological tests are available as test kits that can be performed in the veterinarian's office while you wait.

There are many important reasons why a dog might be infected with adult heartworms yet no microfilariae can be detected:

- Single sex infections or single worm infections
Younger female worms tend to be resistant to the drugs used to clear adult worms. This means that after the first treatment with anti-heartworm medication, a group of young female worms will be left. If antigen testing is not performed, you could be misled into thinking that the infection had been completely cleared.
- Immunologic destruction of microfilariae
In cats, the period in which microfilariae can be detected in the blood stream is extremely short as the immune system rapidly groups and clears these larval worms.
- The dog is taking heartworm prevention medication

Milbemycin, ivermectin, moxidectin, and selamectin are able to kill circulating microfilariae (but not adult heartworms). If for some reason, a dog is not properly tested and has missed a dose of medication, it is possible for an infection to establish yet no microfilariae will be detected. People commonly ask why they must continue annual testing in animals that are on preventive medication; this is one reason. Since *Dipetalonema microfilariae* can be mistaken for heartworm larvae and since microfilariae can be transferred to unborn puppies (but adult heartworms cannot), it is felt by many specialists that no microfilaria positive dog should be treated for heartworm without a positive antigen test.

Antibody Testing

Antigen tests have limited usefulness when it comes to infections involving only a few worms. One problem is that the antigens detected by the tests are unique to female worms. For most tests, at least three female worms are needed for the test to show a positive result. Animals infected with only male worms will test antigen negative. To get around these limitations, antibody tests have been developed to detect the host's immune response against the parasite. This kind of breakthrough has been especially important in testing for cats in whom infection with one or two worms is the usual situation. Antibody testing may be able to detect infection sooner than can antigen testing and infections involving only male worms can be readily detected. As a general rule, antigen tests are performed for dogs with or without a microfilaria test and cats get antibody tests sometimes with antigen tests as well.

How often Should a Dog be Tested?

This is a hard question to answer. With differences in weather patterns every year (i.e. early spring one year, late freeze another year, etc.), it becomes difficult to figure out in what month heartworm preventive medication should be initiated. If there is any question about when the last possible transmission date was in the previous season, it is probably a good idea to simply test the dog annually. If there is any question about the dog spitting out any preventive tablets last season, then the dog should be tested before beginning prevention the next season.

If the dog consistently takes monthly heartworm preventive medication all year round, then testing can probably be performed every 2 to 3 years (though an annual physical exam is needed to legally obtain a prescription for medication).

If a dog lives in an area considered not to have heartworm and travels to an area that does, both microfilaria and antigen testing should be performed at least seven months after the last day the dog was in the heartworm endemic area.

For more information on the different medications used in the prevention of heartworm infection, see heartworm prevention.

Radiographs and Ultrasound

In areas where heartworm infection is not common, routine testing is not performed and infection is unlikely to be detected until the dog is sick. In these cases, the infection is picked up during a work-up for heart disease.

Radiographs can be strongly indicative of heartworm infection if they show blunted tortuous pulmonary arteries and enlargement of the right side of the heart (the side doing all the extra work to pump blood past the worms).

Ultrasound not only can measure thickening of the right side of the heart but can show the live worms wiggling.

When imaging tests are consistent with heartworm disease, antigen and/or microfilaria testing would be the obvious next step.

Heartworm Treatment

It has been said that the treatment of heartworm infection is somewhat of an art. There are several strategies that can be used depending on the dog's medical condition including the option of not treating at all. The important concept to realize is that harsh arsenic-based drugs are necessary to kill adult heartworms and that treating for heartworm infection is neither simple nor safe in itself. What are some of the dangers and options in clearing the body of this parasite?

Patient Evaluation

Prior to therapy, the heartworm patient is assessed and rated for risk into one of four categories. Important factors include: how many worms are thought to be present based upon the tests performed, the size of the dog; the age of the dog; concurrent health factors; severity of the heart disease; and the degree to which exercise can be restricted in the recovery period. Some hospitals use computerized formulas to categorize heartworm infected patients. The categories into which patients are grouped are as follows:

- Class I: Lowest Risk. Young healthy dogs with minimal disease evident on radiographs, normal blood work, and no symptoms of illness. They may cough only occasionally if ever, they only fatigue with exercise, and their chest radiographs are normal.
- Class II: Moderately Affected. Healthy dogs with minimal signs as above, occasional coughing, fatigue only with exercise but with radiographs that show definite evidence of heart disease. Lab testing shows mild anemia, urine dipsticks show some protein, but not severe urinary protein loss.

- Class III: Severely Affected. Dog is suffering from weight loss, cough, difficulty breathing, blatant damage to the vasculature is apparent on radiographs, laboratory work reveals a more severe anemia and marked urinary protein loss.
- Class IV: Caval Syndrome. Dog is collapsing in shock and dark brown urine is evident. Heartworms visible by ultrasound in the AV valve of the right side of the heart, and blood work is very abnormal. These dogs are dying and can only be saved by the physical removal of adult heartworms via an incision through the jugular vein. If such a dog can be saved from this crisis, further heartworm infection treatment cannot be contemplated until the dog is stable enough to fit into one of the other categories above.

After knowing what class the patient fits in, treatment can be determined. Dogs have three groups of heartworms in their body:

- The microfilariae, which are the newborn children of the adult worms living in the heart and pulmonary arteries. The microfilariae are swimming freely in the bloodstream, possibly in large numbers, and it is the microfilariae that can spread to other dogs through a mosquito. The microfilariae are killed so as to keep the dog from spreading the infection.
- The new arrival heartworm larvae, delivered from mosquito bites in the last 6 to 7 months. These are L3 and L4 larvae living in the skin (having arrived within the last 3 months). These will continue their maturation and repopulate the heart and pulmonary arteries if they are not killed before the adult worms.
- The L5 larvae and adult worms living inside the heart and pulmonary arteries. This group requires the arsenic compounds for destruction while the other two groups can be killed with less toxic products.

Killing the Microfilaria and Migrating Worms

The first step in treatment is clearing the migrating immature worms. If we were to jump directly to killing the adult worms first, the adult worms we remove could be readily replaced shortly afterwards by those that were in the process of migration at the time of treatment. By addressing the migrating immature worms first, we minimize the number of adult worms we must kill in the second step. Fewer adult worms dying at once means less risk.

Happily, the microfilariae, L3, and L4 larvae can all be killed by monthly ivermectin-based heartworm preventive products (i.e. Heartgard®, Tri-Heart® etc.). The milbemycin based products (Sentinel® and Interceptor®) will also do the same job but will kill the microfilariae much faster, which can create circulatory shock if there are large numbers of microfilariae dying all at one time. The newer products using selamectin and moxidectin do not clear microfilaria well enough to be used in the treatment of an active infection, so right now the ivermectin based products seem to be the best for this use. The American Heartworm Society recommends 1 to 3 months of a preventive prior to treating the adult worms. How long you choose to wait depends on how urgent the dog's need is to have the adult worms removed. After all, it is the adult worms that cause heartworm disease, not the immature worms addressed by the preventives.

Killing the Adult Worms

The only product currently available for the treatment of adult heartworms is melarsomine dihydrochloride (Immiticide® by Merial). If you follow the manufacturer's recommendations, treatment can be done in two doses or three doses depending on the class of infection. Most universities, however, opt to treat all patients with the three-dose protocol as it creates a more gradual kill of the adult worms, which is safer in terms of embolism and shock.

The patient receives an intramuscular injection deeply in the lower back muscles as shown above. This is a painful injection with a painful substance, and it is common for the patient to be quite sore afterwards at home. Pain medication may be needed. Be careful of the injection site as it may hurt enough to cause a dog to bite. An abscess may form at the site, which requires use of warm compresses. Approximately 30% of dogs experience some sort of reaction at the injection site that resolves in 1 to 4 weeks. Some dogs develop a permanent firm lump at the site of injection.

In the two-dose protocol, the dog receives a second injection the next day on the opposite side of the lower back. In the three-dose protocol, the dog comes back one month later for two doses 24 hours apart (the first dose represents an introductory treatment to kill some of the more sensitive worms.) Keep in mind, too many worms dying at once creates circulatory shock.

After treatment, the patient must be strictly confined for one month following the final treatment. No walks, no running around. The dog must live the indoor life. The reason for this is that embolism to some degree is inevitable and it is important to minimize embolism-related problems. Exercise increases heart rate and oxygen demand and we need the heart to rest during this recovery period. Watch for:

- Coughing
- Fever
- Nose bleeds

If any of these occur, report them to the vet as soon as possible. The most critical time period is 7 to 10 days following a melarsomine treatment, but these signs can occur anytime in the following month.

Ivermectin Only

Melarsomine treatment is expensive and often out of reach for rescue groups, shelters, and many individuals. If the dog is stable (Class I), one option is to simply leave the dog on an ivermectin-based preventive. This option has led to a great deal of misconception about the ability of ivermectin to kill adult heartworms. Let us lay the rumors to rest now:

- Ivermectin does not kill adult heartworms.
- Ivermectin does shorten the lifespan of adult heartworms.
- Ivermectin does sterilize adult heartworms.
- Ivermectin does kill microfilaria (keeping the dog from being a source of contagion)
- Ivermectin does kill L3 and L4 larvae (preventing new infections).

This means that if you opt to treat a heartworm positive dog with an ivermectin heartworm preventive only, you can expect the dog to remain heartworm positive for a good two years and the heartworm disease will be progressing during those two years. This is not good for the dog but certainly beats getting no treatment of any kind. This approach should only be considered for patients who are Class I and may be able to withstand two years of heartworm infection.

What is Wolbachia?

Wolbachia is a genus of rickettsial organisms, sort of like bacteria but not exactly. They live inside the adult heartworm. These organisms seem to be protective or beneficial to the heartworms; treating the dog with the antibiotic doxycycline, which kills *Wolbachia*, seems to sterilize female heartworms, meaning they cannot reproduce. *Wolbachia* is also thought to be involved in the embolism and shock those results when heartworms die. The role of this organism is still being investigated. If your veterinarian wants to pre-treat your heartworm positive dog with doxycycline, it may be because of concerns regarding this organism. As new information emerges, we will post here.

Heartworm: The Parasite

By Wendy C. Brooks DVM, DABVP

Heartworm (*Dirofilaria immitis*) is a fairly large worm, up to 14 inches long, that in adulthood lives in the heart and pulmonary arteries of an infected dog. Dogs acquire this infection through mosquito bites as mosquitoes readily pick up larval heartworms from infected dogs and carry them to new dogs. Some geographic areas have severe heartworm problems while other areas have virtually none. In order for the parasite to establish its presence in an area, the following conditions must be met:

- Types of mosquitoes capable of carrying larval heartworms must be present.
- The weather must be warm enough to allow heartworm larval development within the mosquito.
- There must be infected dogs (or coyotes) in the area.
- There must be vulnerable host dogs in the area.

When these conditions come together, an area becomes endemic for heartworm disease.

The detailed version of the heartworm story:

Let's follow the worm's life cycle.

The Adult Heartworm

Blood going to the lung to pick up oxygen is received first by the right atrium of the heart, then sent to the right ventricle (the pumping chamber) and then sent out to the lung via the pulmonary arteries. This path is outlined in the blue pathway in the graphic below.

The adult heartworm is fairly large, several inches in length, and it prefers to live, not in the heart, but in the pulmonary arteries. It swims into a cozy tubular artery, where it is massaged and nourished by the blood coursing past it. In the pulmonary arteries of an infected dog, the worm's presence generates a strong inflammatory response and a tendency for blood to inappropriately clot. If enough worms are present, the heart must work extra hard to pump blood through the plugged up arteries.

If the worm infection is a heavy one (over 25 worms for a 40 lb dog), the worms begin to back up into the heart's right ventricle (the chamber which pumps blood through the lung). The worms actually take up a significant amount of space within the heart, space that could have been taken up by blood. With less blood going through the heart, there is less blood being pumped out to the lung. When over 50 worms are present, the ventricle is completely full and the atrium, the chamber receiving blood from the rest of the body, begins to fill with worms.

When over 100 worms are present, the entire right side of the heart is filled with worms and there is very little room for any blood to be pumped. This drastic phenomenon is called "Caval Syndrome" and most dogs do not survive it.

Microfilariae (First Stage Larvae)

With adult male and female worms present, mating begins to occur. Heartworms do not lay eggs like other worm parasites; instead they give live birth and the baby worms are called microfilariae.

Microfilariae are released into the circulatory system in hopes that they will be slurped up by a mosquito taking a blood meal and carried to a new host. Microfilariae may live up to two years within the host dog in whom they were born. If, after this period, a mosquito has not picked them up, they die of old age. Microfilariae may also be transmitted across the placental barrier to unborn puppies if the mother dog is infected with heartworm. It is important to realize that such puppies will not develop adult heartworms or heartworm disease from these microfilariae; in order for a heartworm to reach adulthood, it must be passed through a mosquito. Parasitic worms have 5 larval stages and are termed L1, L2, L3, etc. Heartworm microfilariae are first stage larvae: L1s.

Note: Ivermectin, and milbemycin based heartworm preventives will kill microfilariae after prolonged use. Dogs on these heartworm preventives, even if infected with adult heartworms, will not test positive for microfilariae. Moxidectin based heartworm preventives (Advantage Multi®) and selamectin based heartworm preventives (Revolution®) will not reliably wipe out microfilariae; infected dogs who have received these products may or may not test positive.

Inside the Mosquito

So, let us continue to follow the young heartworm's development inside the mosquito who has taken it in with a blood meal. Within the mosquito's body, the microfilariae will develop to L2's and finally to L3's, the stage capable of infecting a new dog. How long this takes depends on the environmental conditions. In general, it takes a few weeks. A minimum environmental temperature of 57 degrees F is required throughout this period. The process goes faster in warmer weather.

Infesting a New Dog

When a dog is bitten by an infected mosquito, the L3 is not deposited directly into the dog's bloodstream. Instead, it is deposited in a tiny drop of mosquito "spit" adjacent to the mosquito bite. For transmission to occur there must be adequate humidity to prevent evaporation of this fluid droplet before the L3's can swim through the mosquito bite and into the new host.

Once safely inside the new host, the L3 will spend the next week or two developing into an L4 within the host's skin. The L4 will live in the skin for three months or so until it develops to the L5 stage and is ready to enter the host's circulatory system. The L5, which is actually a young adult, migrates to the heart and out into the pulmonary arteries (if there is room) where it will mate, approximately 5 to 7 months after first entering the new host.

Note: All commercially available heartworm preventives act by wiping out the freshly delivered L3's and the L4's living in the skin. The ivermectin products are also able to kill the younger L5's.

Also note: because the heartworm tests on the market either look for microfilariae or for adult worm proteins, they will not detect infection with immature worms. This is why it takes 5 to 7 months from the time of exposure to get a valid heartworm test and this is also why there is no point in testing puppies less than 5 to 7 months of age.