

Fairleigh Pet Center
1212 Bardstown Rd.
Louisville, KY 40204

CANINE HEARTWORM DISEASE

What causes heartworm disease?

Heartworm disease or dirofilariasis is a serious and potentially fatal disease in dogs. It is caused by a blood-borne parasite called *Dirofilaria immitis*.

Heartworms are found in the heart and adjacent large blood vessels of infected dogs. The female worm is 6 to 14 inches long (15 to 36 cm) and 1/8 inch wide (5 mm). The male is about half the size of the female. One dog may have as many as 300 worms.



How do heartworms get into the heart?

Adult heartworms live in the heart and pulmonary arteries of infected dogs. They have been found in other areas of the body, but this is unusual. They live up to five years and, during this time, the female produces millions of offspring called microfilaria. These microfilariae live mainly in the small vessels of the bloodstream. The immature heartworms cannot complete their life cycle in the dog. The mosquito is required for some stages of the heartworm life cycle. The microfilaria are not infective (cannot grow to adulthood) in the dog – although they do cause problems.

As many as 30 species of mosquitoes can transmit heartworms. The female mosquito bites the infected dog and ingests the microfilariae during a blood meal. The microfilariae develop further for 10 to 30 days in the mosquito and then enter the mouthparts of the mosquito. The microfilariae are now called infective larvae because at this stage of development, they will grow to adulthood when they enter a dog. The mosquito usually bites the dog where the hair coat is thinnest. However, having long hair does not prevent a dog from getting heartworms.

When fully developed, the infective larvae enter the bloodstream and move to the heart and adjacent vessels where they grow to maturity in two to three months and start reproducing, thereby completing the full life cycle.

Where are heartworms found?

Canine heartworm disease occurs all over the world. In the United States, it was once limited to the south and southeast regions. However, the disease is spreading and is now found in most regions of the United States and Canada, particularly where mosquitoes are prevalent.

How do dogs get infected with them?

The disease is not spread directly from dog to dog. An intermediate host, the mosquito, is required for transmission. Spread of the disease therefore coincides with mosquito season. The number of dogs infected and the length of the mosquito season are directly correlated with the incidence of heartworm disease in any given area.

It takes a number of years before dogs show outward signs of infection. Consequently, the disease is diagnosed mostly in four to eight year old dogs. The disease is seldom diagnosed in a dog less than one year of age because the young worms (larvae) take up five to seven months to mature after infection.

What do heartworms do to the dog?

Adult heartworms: Adult heartworms cause disease by clogging the heart and major blood vessels leading from the heart. They interfere with the valve action in the heart. By clogging the main blood vessels, the blood supply to other organs of the body is reduced, particularly blood flow to the lungs, liver and kidneys, leading to malfunction of these organs.

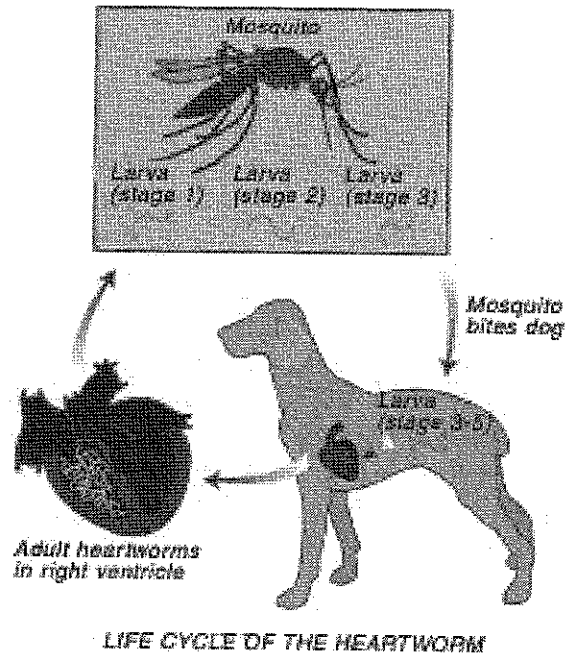
Most dogs infected with heartworms do not show any signs of disease for as long as two years. Unfortunately, by the time clinical signs are seen, the disease is well advanced. The signs of heartworm disease depend on the number of adult worms present, the location of the worms, the length of time the worms have been present, and the degree of damage to the heart, lungs, liver, and kidneys from the adult worms and the microfilariae.

The most obvious signs are a soft, dry cough, shortness of breath, weakness, nervousness, listlessness, and loss of stamina. All of these signs are most noticeable following exercise, when some dogs may even faint.

Listening to the chest with a stethoscope will often reveal abnormal lung and heart sounds. In advanced cases, congestive heart failure may be apparent and the abdomen and legs will swell from fluid accumulation. There may also be evidence of weight loss, poor condition, and anemia.

Severely infected dogs may die suddenly during exercise or excitement.

Microfilariae (Young heartworms): Microfilariae circulate throughout the body but remain primarily in the small blood vessels. Because they are as wide as the small vessels, they may block blood flow in these vessels. The body cells being supplied by these vessels are deprived of the nutrients and oxygen normally supplied by the blood. The lungs and liver are primarily affected.

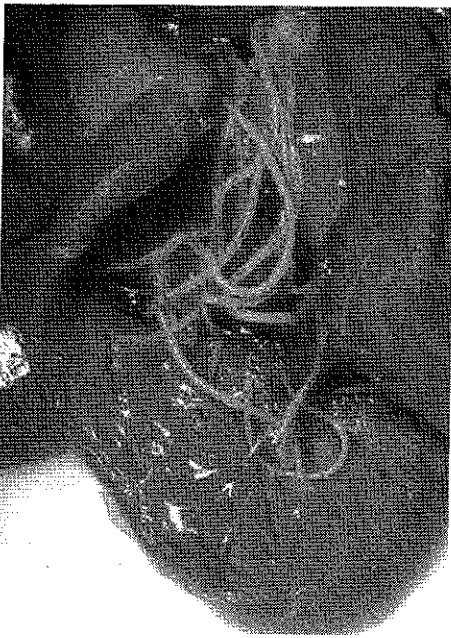


Destruction of lung tissue leads to coughing. Cirrhosis of the liver causes jaundice, anemia, and general weakness because this organ is essential in maintaining a healthy animal. The kidneys may also be affected and allow poisons to accumulate in the body.

How is heartworm infection diagnosed?

In most cases, diagnosis of heartworm disease can be made by a blood test that can be run in the veterinary hospital or by a veterinary laboratory. Further diagnostic procedures are essential to determine if the dog can tolerate heartworm treatment. Depending on the case, we will recommend some or all of the following procedures before treatment is started.

Serological test for antigens to adult heartworms: This is a test performed on a blood sample. It is the most widely used test because it detects antigens (proteins) produced by adult heartworms. It will be positive even if the dog does not have any microfilariae in the blood. This occurs in about 20% of the cases. Dogs with less than five adult heartworms will not have enough antigen to give a positive test result, so there may be an occasional false negative result in dogs with early infections. Because the detected antigen is only produced by the female heartworm, a population of only male heartworms will also give a false negative. Therefore, there must be at least five female worms present for the most common heartworm test to diagnose heartworm disease.



Blood test for microfilariae: A blood sample is examined under the microscope for the presence of microfilariae. If microfilariae are seen, the test is positive. The number of microfilariae seen gives us a general indication of the severity of the infection. However, the microfilariae are seen in greater numbers in the summer months and in the evening, so these variations must be considered. Approximately 20% of dogs do not test positive even though they have heartworms because of an acquired immunity to this stage of the heartworm. Because of this, the antigen test is the preferred test. Also, there is another blood parasite that is fairly common in dogs that can be hard to distinguish from heartworm microfilariae.

Blood chemistries: Complete blood counts and blood tests for kidney and liver function may give an indication of the presence of heartworm disease. These tests are also performed on dogs diagnosed as heartworm-infected to determine the function of the dog's organs prior to treatment.

Radiographs (X-rays): A radiograph of a dog with heartworms will usually show heart enlargement and swelling of the large artery leading to the lungs from the heart. These signs are considered presumptive evidence of heartworm disease. Radiographs may also reveal the condition of the heart, lungs, and vessels. This information allows us to predict an increased possibility of complications related to treatment.

Electrocardiogram: An electrocardiogram (EKG or ECG) is a tracing of the electric currents generated by the heart. It is most useful to determine the presence of abnormal heart rhythms.

Echocardiography: An ultrasonic examination that allows us to see into the heart chambers and even visualize the heartworms.

How are dogs treated for heartworms?

There is some risk involved in treating dogs with heartworms, although fatalities are rare. In the past, the drug used to treat heartworms contained arsenic so toxic effects and reactions occurred more frequently. A newer drug is now available that does not have the toxic side-effects, allowing successful treatment of more than 95% of dogs with heartworms.

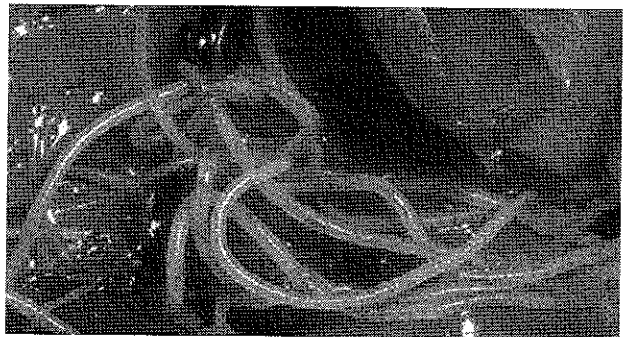
Some dogs are diagnosed with advanced heartworm disease. This means that the heartworms have been present long enough to cause substantial damage to the heart, lungs, blood vessels, kidneys, and liver. A few of these cases will be so advanced that it will be safer to treat the organ damage rather than risk treatment to kill the heartworms. Dogs in this condition are not likely to live more than a few weeks or months.

Treatment to kill adult heartworms: An injectable drug to kill adult heartworms is given. It kills the adult heartworms in the heart and adjacent vessels. These injections may be divided and given thirty days apart.

Complete rest is essential after treatment: The adult worms die in a few days and start to decompose. As they break up, they are carried to the lungs, where they lodge in the small blood vessels and are eventually reabsorbed by the body. This can be a dangerous period so it is absolutely essential that the dog be kept quiet and not be allowed to exercise for one month following treatment. The first week after the injections is critical because the worms are dying. A cough is noticeable for seven to eight weeks after treatment in many heavily infected dogs.

Prompt treatment is essential if the dog has a significant reaction in the weeks following the initial treatment, although such reactions are rare. If a dog shows loss of appetite, shortness of breath, severe coughing, coughing up blood, fever, and/or depression, you should notify us. Response to antibiotics, cage rest, and supportive care and intravenous fluids is usually good in these cases.

Treatment to kill microfilaria: Approximately one month following treatment to kill the adults, the dog is returned to the hospital for administration of a drug to kill the baby heartworms or microfilariae. Your dog needs to stay in the hospital for the day. Your dog is started on heartworm preventive after this treatment.



Other treatments: In dogs with severe heartworm disease, it may be necessary to treat them with antibiotics, special diets, diuretics to remove fluid accumulations, and drugs to improve heart function prior to treatment for the heartworms.

Dogs with severe heart disease may need lifetime treatment for the heart failure, even after the heartworms have been killed. This includes the use of diuretics, heart drugs, and special low salt, low protein diets.

Response to treatment: Dog owners are usually pleasantly surprised at the change in their dog following treatment for heartworms, especially if the dog had been showing signs of

heartworm disease. The dog has a renewed vigor and vitality, improved appetite, and weight gain.

Are changes made in the treatment protocol for dogs that have severe heartworm disease?

Yes. The state of heart failure is treated as described above. However, we also treat the adult heartworms in a two-stage process. Only one treatment with the drug to kill the worms is given initially. This causes the death of approximately half of the worms. One month later, the full treatment is given to kill the remaining worms. By killing them in two stages, the severe effects on the lungs are much less likely to occur. This protocol is also used in moderate cases to provide a safer treatment.

How can I prevent this from happening again?

When a dog has been successfully treated for heartworms, it is essential to begin a heartworm prevention program to prevent future recurrence. With the safe and affordable heart preventives available today, no pet should ever have to endure this dreaded disease.

*This client information sheet is based on material written by Ernest Ward, DVM.
© Copyright 2005 Lifelearn Inc. Used with permission under license. November 15, 2012*

The Pet Health Care Library

Heartworm: The Parasite

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:

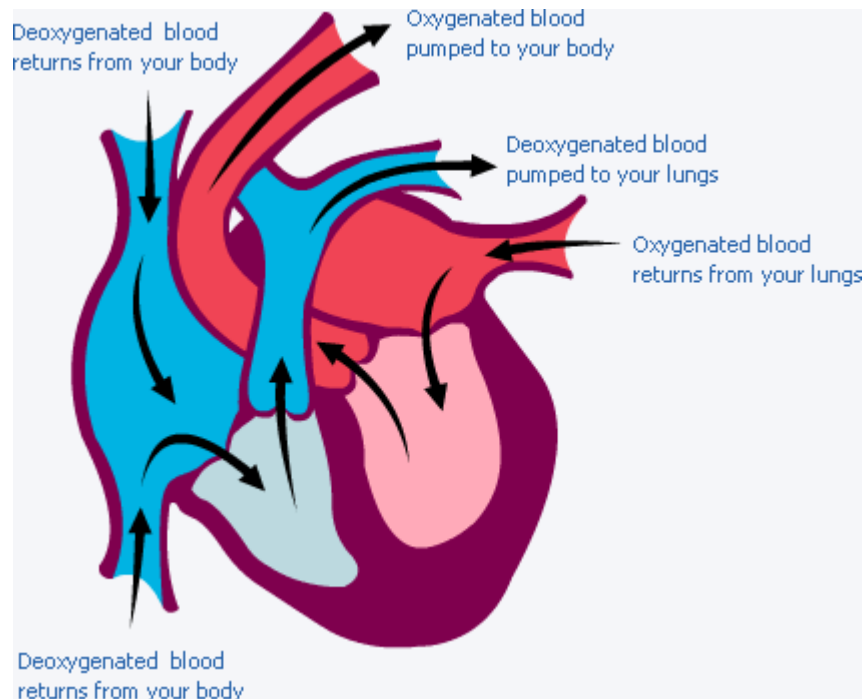
- Types of mosquitoes capable of carrying larval heartworms must be present.
- The weather must be warm enough to allow heartworm larval development within the mosquito.
- There must be infected dogs (or coyotes) in the area.
- There must be vulnerable host dogs in the area.

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.



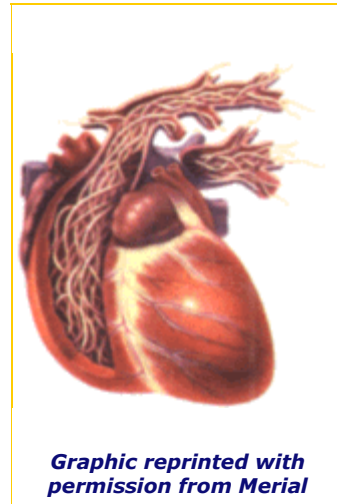
The adult heartworm is fairly large, several inches in length, and it prefers to live, not in the heart, but in the pulmonary arteries. It swims into a cozy tubular artery, where it is massaged and nourished by the blood coursing past it. In the pulmonary arteries of an infected dog, the

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.

Infecting 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.

Pet Pharmacy

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

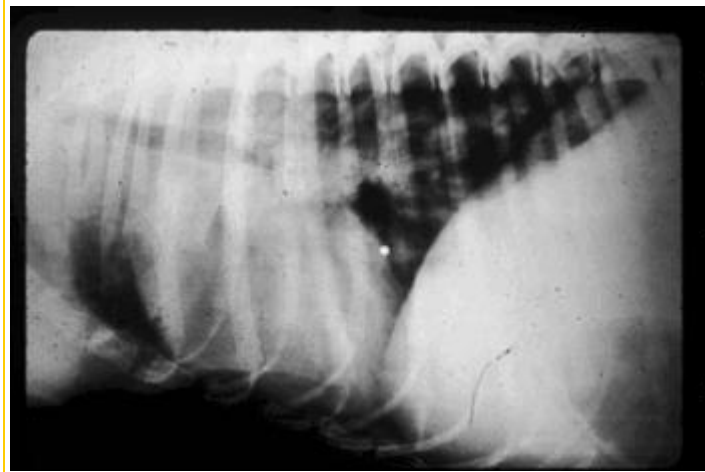
Prior to therapy, the heartworm patient is assessed and rated for risk into one of four categories. Important factors include: how many worms are thought to be present based upon the tests performed, the size of the dog; the age of the dog; concurrent health factors; severity of the heart disease; and 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:



Chest radiograph from a mildly affected dog

- 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.





Chest radiograph from a severely affected dog

- 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 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.

See a video of the physical [removal of adult heartworms](#) from the jugular vein of a dog with caval syndrome.

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 microfilarias 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 deep 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 would require 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, to some degree, 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.

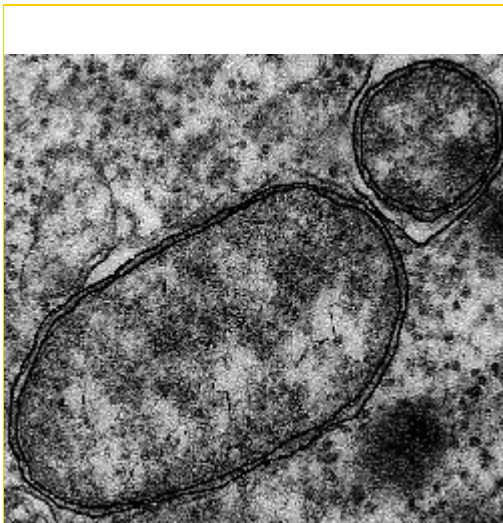
Ivermectin Only

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-based heartworm preventive only, you can expect the dog to remain heartworm positive for as long as 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 prolonged heartworm infection.

What is *Wolbachia*?



Micrograph of a Wolbachia organism.

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 that result 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.

Copyright 2011 - 2012 by the Veterinary Information Network, Inc. All rights reserved.

The Pet Health Care Library Preventing Heartworm Infection in Dogs (Chemoprophylaxis)

Brands:

Ivermectin-based Products: Heartgard, Heartgard Plus, Iverhart Plus, Iverhart Max, Tri-Heart Plus

Milbemycin-based Products: Interceptor, Sentinel

Selamectin-based Products: Revolution

Moxidectin-based Products: Advantage Multi, Proheart6

Heartworm preventive medications are used to periodically kill larval heartworms that have managed to gain access to the dog's body. At this point, the products available are intended for monthly use. This means that they kill all the heartworm larvae (stage L3 and L4) that have accumulated in the past month each time they are given. Some products offer the ability to kill older larvae which helps keep the pet protected in case someone is late giving the heartworm preventive medication at some point. There are presently many choices, both topical and oral, plus, while the subject of this page is canine heartworm prevention, all the products discussed have feline formulations.

Ivermectin-based Products:

***Heartgard, Heartgard Plus made by Merial
Iverhart Plus, Iverhart Max made by Virbac
Tri-Heart Plus made by Schering Plough***

The approval of ivermectin in 1987 represented a huge breakthrough in heartworm prevention. Preventive medication for the first time could be given once a month instead of every day. These monthly medications utilize an extremely low dose of ivermectin that is adequate to kill any L3 and L4 larval stages inhabiting the pet's skin tissues at the time the medication is given. In other words, infection takes place but is halted every month when the medication is administered.

If Given to a Heartworm Positive Dog by Accident

In most cases, no reaction of any kind occurs when an ivermectin-based heartworm preventive is given to a heartworm-positive dog.

In fact, giving an ivermectin-based heartworm preventive to an infected dog is the first step in heartworm treatment. Ivermectin kills the developing larval worms and clears the circulating microfilariae, thus rendering the dog unable to spread its infection and minimizing the number of adult worms to be killed in the second phase of treatment when the adult worms are specifically addressed.

If the larval worms die too quickly, a shock-like circulatory reaction can occur so for this reason the American Heartworm Society recommends that the first dose of ivermectin be given under veterinary supervision. This allows the dog to be observed for several hours following the oral dose in case of trouble. That said, in most cases no reaction of any kind occurs and the larval worms are cleared without event. This does mean, however, that giving this product to a dog with heartworm will kill all circulating microfilariae and the dog will test erroneously heartworm negative by Diful or Knott testing. (ELISA test kits should still be accurate). In addition to killing microfilariae, ivermectin will also suppress reproduction in the adult female worms and shorten the overall life span of adult worms. Ivermectin does not kill adult heartworms (just the immature ones) although, as said, it

cuts their life expectancy.

The Reach Back Effect

There is also a phenomenon called the reach back effect. This means that if a dog goes off heartworm preventive medication for a prolonged period (four months was the time tested), re-starting preventive could still curb adult heartworm infection in the heart and pulmonary arteries. In the 1988 experiment by Atwell, dogs who went off heartworm preventive for four months and then restarted with ivermectin had 95% fewer adult heartworms than dogs who went without ivermectin, although it should be noted that some heartworms were still able to establish infection. This means that if you skip several doses of ivermectin accidentally, it is still worth picking up where you left off.

Other Parasites Covered

Ivermectin at the heartworm preventive dose is not strong enough to kill common intestinal parasites. Because of this fact, [pyrantel pamoate](#), a dewormer, was added to cover [hookworms](#) and [roundworms](#) in the original Heartgard product. As other ivermectin-based products have entered the market, these have also added pyrantel pamoate to extend the spectrum of protection.

[Whipworms](#) are not covered by any of the ivermectin-containing products at this time, but in order to remain competitive in the market, manufacturers may pay for treatment for whipworm infections acquired while their product is administered. The products containing both ivermectin and pyrantel pamoate are Heartgard Plus, Iverhart Plus, and Tri-Heart Plus. Iverhart Max includes both pyrantel pamoate and [praziquantel](#) so as to cover tapeworms as well.

Breed Sensitivity

There are breed-related sensitivities with ivermectin (i.e. collie-related breeds have some difficulties) though at the low doses used in the prevention of heartworm disease are not a problem for any breed.

Use of Large Animal Products

It is neither safe nor legal to obtain large animal ivermectin products for use in dogs for heartworm prevention. Discussions of doses have circulated around the Internet and in other sources advocating the use of highly concentrated ivermectin formulas for heartworm prevention in dogs. These doses are not comparable to the miniscule doses in licensed heartworm preventive products and using them represents an element of gambling. Large animal ivermectin products are vastly more concentrated than those meant for dogs and it becomes problematic to dilute them properly. Even small doses of these products are unnecessarily high and if they are inadvertently given to a sensitive individual, death can result.

For information on these products from their manufacturers visit:

<http://heartgard.us.merial.com/home/>

www.iverhart.com

www.triheartplus.com

Milbemycin Oxime-based Products

Interceptor & Sentinel made by Novartis

This product is also given monthly, also clears microfilariae, acts by killing all L3s and L4s

accumulated in the month prior to administration, and will suppress female worm's ability to reproduce. There are a few important differences to note between this product and the ivermectin-based products, though.

If Given to a Heartworm Positive Dog by Accident

If milbemycin is inadvertently given to a dog who has active heartworm infection, the microfilariae are killed much faster than with the ivermectin products. This might sound like a good thing but in fact it increases the likelihood of the previously mentioned shock-like reaction when all the first stage larvae die at once. In a dog with a light infection this might not be important, but in a heavily infected dog it is safer not to use milbemycin to clear the microfilariae.

Of course, heartworm preventives are meant to be used in heartworm negative dogs. If these products are used according to their labeled instructions, this issue should never arise. Milbemycin-based preventives are safe and highly effective in preventing heartworms in dogs that are heartworm negative to begin with.

The Reach Back Effect

When milbemycin is given to a dog after a prolonged period without heartworm preventive (the Atwood experiment), the dog is expected to have 41% fewer heartworms than if heartworm prevention was not resumed. This was not as good a result as with the ivermectin products because ivermectin is better at killing older heartworm larvae. If one finds oneself in the situation of having skipped several months of heartworm prevention in the middle of heartworm season, one might do better to restart an ivermectin-based product rather than a milbemycin-based product.

Other Parasites Covered

Milbemycin, however, does not require the addition of other dewormers in order to provide a broad spectrum of parasite control. The milbemycin products control roundworms, hookworms, and whipworms without the addition of a second parasiticide. Milbemycin is also available combined with [lufenuron](#) for the control of fleas in the form of Sentinel. Lufenuron is an oral flea sterilizer that prevents any fleas feeding on the dog from laying viable eggs.

Milbemycin can also be used in the treatment of [demodectic mange](#). A specific dosing schedule is needed to accomplish this; heartworm preventive doses are not adequate but milbemycin does offer a convenient treatment option for collie-type breeds.

There are no breed-related sensitivities for milbemycin.

For more information on Interceptor or Sentinel, see the [Novartis Animal Health heartworm](#) section.

Selamectin-based Products: *Revolution made by Pfizer*

Ivermectin's entrance onto the anti-parasite warfront represented a culmination in the trend for broader and broader spectrum parasite control. Selamectin is a closely related cousin of ivermectin. It is designed for broad coverage of small animal parasites and will protect dogs not only against heartworm but also against ear mites, sarcoptic mange mites, ticks, and fleas. Cats are protected against heartworm, fleas, ear mites, roundworms, and hookworms. The product is topical, applied monthly and is fully approved for safe use in heartworm infected animals. Selamectin is not as effective at clearing microfilariae as other

products and thus is not generally used in the treatment of active heartworm infections.

See more information on [Revolution](#) from the manufacturer.

Moxidectin-based Products:
Advantage Multi made by Bayer
Proheart6 made by Fort Dodge

Moxidectin is another relative of ivermectin. In 2007 it was combined with imidacloprid, the active ingredient in Advantage, to create a broad spectrum topical for dogs and cats. The product prevents heartworm infection, kills roundworms, hookworms, and whipworms. The imidacloprid will kill the pet's fleas. As with selamectin, it can be given to heartworm positive dogs and it will decrease the number of circulating microfilariae but it is not a good choice in the treatment of active heartworm disease.

Moxidectin is available in Australia and Europe in a long-acting injectable form that is given once a year for heartworm prevention. A similar product, Proheart6, was previously available in the U.S. but it was withdrawn from the market due to adverse events. The long-acting products were developed to address the problem of accidental failure to administer the preventive on schedule. Since adverse events have not been problematic in Australia or Europe, it is possible that this mode of heartworm prevention may return to the U.S. as there is the potential to prevent a great deal of heartworm infection. Currently, however, the only moxidectin product available for small animals in the U.S. is Advantage Multi, which is given once a month as a topical.

See more information on [Advantage Multi](#).

Proheart6 is an injection given once every six months, obviating the need for the owner to remember to use a monthly product. The moxidectin is contained in "microspheres," enabling the drug to last a full six months (or in the case of the Australian version of the same product, a larger volume is given and it lasts 12 months). In other countries, Proheart6 rapidly captured 40-50% of the entire heartworm prevention market but in this country, it was voluntarily withdrawn from the market in 2004 after a number of adverse reactions were reported. There has been great deal of controversy regarding these adverse reaction reports, especially since similar reactions have not been reported in the international market using the identical product made in the same manufacturing plant as the U.S. product. In June of 2008, Proheart6 returned to the U.S. market with some restrictions so that true reactions to the product can be tracked and not confused with other diseases or reactions to other medications. The FDA is studying the situation. The current restrictions are up for review in one year.

The restrictions in place are:

- All veterinarians prescribing Proheart6 must receive specific certification.
- Proheart6 may not be used in dogs under age 6 months or over age 7 years.
- A baseline blood panel is required prior to injection to rule out concurrent illness that could be confused with a drug reaction.
- The Proheart6 injection may not be given within 30 days of vaccination (to rule out any confusion between adverse drug reaction and vaccine reaction).
- The dog must be negative for heartworm infection before receiving the injection.
- The owner must sign a consent form prior to injection.
- The owner must receive an information sheet provided by Fort Dodge explaining the product and its use.

Proheart6 is also effective in controlling [hookworm](#) infection.

Learn more about [Proheart6](#) made by Fort Dodge Animal Health.

When to Start Giving Heartworm Preventive Each Year?

Obviously the answer to this question is regional. Indeed it may be simplest to just use preventive medications all year round or to see what your regular veterinarian recommends for your area.

There is more to transmission than the simple presence of mosquitoes; it must also be warm enough for a long enough time period to allow the development of microfilariae to infect L3s within the mosquito's body. A simple formula involves counting the degrees above 57F reached each day. Each degree is called a heartworm development unit and when 234 heartworm development units have accumulated within a 30-day period, conditions have been reached that will allow the transmission of L3 heartworm to new hosts. A monthly heartworm pill, chewable, or topical must be given at the end of a month in which 234-heartworm development units has accumulated.

When 30 days pass and 234 heartworm development have not accumulated, mosquitoes will be dying from the cold before any microfilariae they carry can develop to the infective stage. Monthly heartworm preventive needs not be given after a month under these conditions.

If all this sounds complicated, it is. In addition, most of us have better things to do besides monitoring average weather temperatures. It may be simpler to use the product all year round or just go by the recommendations of a practicing veterinarian in the region in question.

Immiticide supplies run dry

August 9, 2011

By: Jennifer Fiala

For The VIN News Service

The only heartworm adulticide approved by the U.S. Food and Drug Administration (FDA) for use in canines is temporarily unavailable, with no known re-release date.

News of the [Immiticide \(melarsomine dihydrochloride\)](#) shortage surfaced last week with an open letter to practitioners from drugmaker Merial that warns of an outage expected to "last several weeks to months." The letter, dated Aug. 4, asked practitioners to help conserve Merial's dwindling Immiticide supplies by ordering product only to treat dogs with severe heartworm infestation. However, the notice of the shortage caused a run on remaining stock. The company's technical services department confirmed today that Merial is "officially out" of the drug.

"After mailing the Dear Doctor letter we experienced an unprecedented surge in Immiticide orders and depleted inventory much more rapidly than anticipated," explains Natasha Mahanes, a Merial spokeswoman.

Immiticide availability has been [shaky since early last year](#), when Merial, the animal health arm of Sanofi, reported that its U.S. supplier could no longer obtain the product's active ingredient, and the FDA was hesitant to allow Merial's overseas supplier to fill American orders. As a result, Merial stopped allowing veterinarians to simply order and stock the drug in an effort to conserve U.S. supplies and implemented a "restricted distribution program." Translation: Veterinarians treating only severe cases of heartworm disease could access the drug on a case-by-case basis with approval from the company.

In an email exchange with the VIN News Service, Mahanes noted that Merial's latest Immiticide supply problems are not tied to the troubles of 2010. Rather, it is "a new and separate manufacturing challenge," she writes.

"This situation is related to technical issues providing finished product to us. The finished product is made by a manufacturing company in the U.S.," she explains. "... We are working diligently to mitigate this situation, and there is a possibility that an alternate source of supply may be identified."

That's encouraging news for veterinarians such as Dr. Skip Fix, a practitioner in Houston. With two boxes of Immiticide left in his clinic, Fix is pondering how best to ration it.

"At this moment I have a 50-pound dog that I'm going to treat," he says. "There are five bottles to a box, and he's going to need two-and-a half of them. We're trying to find out from the shelter near us if they need the remainder for a small dog so we can use every last drop of this.

"This shortage could take a month, it could take forever," Fix adds. "I usually have a couple heartworm cases going every week, so it is a concern."

Once his in-house supply runs dry, Fix plans on turning to a heartworm preventative and doxycycline to manage infestation — a protocol supported by the [American Heartworm Society](#), slated soon to release [updated guidance](#) for practitioners on treating heartworm-positive dogs without Immiticide.

Dr. Tom Nelson, a past president of the American Heartworm Society and a practitioner at the Animal Medical Center in Anniston, Ala., notes that the use of doxycycline in combination with heartworm preventive has been shown to reduce pathology, the number of adult worms and the infective potential of microfilaria in canine patients.

"The shortage of Immiticide is unfortunate, but we're going to have to deal with it," he says.

Treating heartworm is tricky business. An infected dog, for example, must not vigorously exercise because an increase in heart rate raises the risk that fragments of dead worms in its blood vessels could cause thromboembolism — the formation of an embolism, in this case of dead worms — to the lungs, which usually presents as acute dyspnea. The condition is treatable with steroids but may prove fatal. Nelson notes that Immiticide quickly kills worms, thereby shortening the time that a dog's exercise must be restricted.

Slow-kill therapies, such as the use of heartworm preventatives, potentially allow for greater opportunity in which worms might block blood vessels, leading to worsened pulmonary pathology.

"Exercise should be restricted during the duration of the treatment. We're normally talking about 12 to 18 months," Nelson says.

The American Heartworm Society: Guidance for Heartworm Disease Management During the Adulticide Unavailability

Background

August 9, 2011: The American Heartworm Society became aware of a pending product unavailability of the only available heartworm adulticide product, IMMITICIDE®, for an undetermined duration.

Because there are no other approved products available for killing adult heartworms, the American Heartworm Society Board and Scientific Committee has developed and approved the following management plan for heartworm positive dogs during this period of adulticide unavailability. While the unavailability persists, heartworm-positive dogs should be managed to achieve three primary goals:

- Reduce potential pathology from the infection.
- Maintain the health of the dog until it can be appropriately treated.
- Prevent additional heartworm infection of the dog.

These goals may be achieved by strict adherence to the following:

- Limit the activity level of the dog to reduce pathology.^{1,2}
- Carefully place the non-protected dog on heartworm prevention.^{3,4,5,6,7}
- Administer doxycycline to reduce pathology and infective potential of heartworms.⁸

The Management Plan: Heartworm-Positive Dogs and Dogs Not Completing a Full Course of Adulticidal Therapy

1. Verify any positive antigen test by performing a second antigen test, sourced from a different manufacturer. If a dog is confirmed antigen positive or for dogs already initiated on, but not completed adulticidal therapy (due to product unavailability), a microfilariae test should be performed. In rare cases, the administration of heartworm preventives to microfilaremic dogs can result in shock-type reaction. For this reason professional observation is **highly** recommended.

- **If microfilariae are detected, the dog should be pretreated with corticosteroids with or without antihistamines⁹ and then administered a dose of heartworm preventive (macrocytic lactone).¹⁰**
 - While all heartworm preventives affect microfilariae, the resulting immunologic reaction of the dog to the microfilariae can vary dramatically.^{3,4,5,6,7} Therefore dogs should be kept under clinical observation for at least 8 hours following the initial dose of heartworm preventive to allow rapid, appropriate medical treatment should a shock reaction occur.
 - **Anti-inflammatory pretreatment:** Dexamethasone at 0.25 mg/kg intravenously and diphenhydramine at 2.2 mg/kg intramuscularly, **or** 1 mg/kg of prednisolone orally 1 hour before and 6 hours after administration of the first dose of preventive.⁹
 - Elimination of every single microfilaria is not the goal; the health, safety, and maintenance of the patient is the goal.

- Microfilariae will **likely** persist following preventive dosing.
 - If the positive dog is already on prevention, continue regular monthly oral or topical dosing or twice yearly injections of preventives.
- **If the dog is negative for microfilariae, a heartworm preventive should be administered.**
- 2. Dogs should then be *maintained* continuously on heartworm preventive to limit further infection of the dog until the adulticide product is again available.**
 - 3. Dogs should also receive doxycycline at 10 mg/kg BID for 4 weeks.** This dosing should be repeated quarterly until adulticide is available. (*Dose may be reduced to 5 mg/kg BID if tolerance issues exist.*)
 - Doxycycline has been demonstrated to affect the viability of subsequent heartworm stages.
 - Microfilariae will still be able to infect mosquitoes, but the infective larvae from these mosquitoes will be less capable of infecting another dog.
 - The doxycycline protocol would be 1 month on, 2 months off, 1 month on, 2 months off, etc.
 - The combination of macrocyclic lactone and doxycycline is proven to be more effective than macrocyclic lactones alone. Research studies have demonstrated macrocyclic lactone/doxycycline combinations will:
 - Shorten the life span, but not eliminate the adult worm infection.
 - Lessen the pathology associated with worm death.
 - Disrupt heartworm transmission.
 - 4. Restrict ALL activity of the dog! Limit ALL exercise!**
 - The severity of heartworm disease is directly related to the activity level of the dog.
 - As physical activity increases, pathology associated with adult heartworms increases.
 - 5. Any dogs that are symptomatic for heartworm infection should be treated medically to relieve signs of respiratory distress.** Surgical options should be weighed for dogs exhibiting cardiovascular compromise.
 - 6. When adulticide product is again available:**
 - Adult heartworms will **likely** persist in the dogs managed under this protocol.
 - Nevertheless, dogs should be retested to revalidate the presence of an adult heartworm infection.
 - If positive, the dog should be appropriately treated for adult heartworms with the approved adulticidal product.

REMEMBER THE GOALS:

- Reduce potential pathology from the infection.
- Maintain the health of the dog until it can be appropriately treated.
- Prevent additional heartworm infection of the dog.

For further background information considered in development of this management protocol, refer to the American Heartworm Society's Current Canine Guidelines under the Veterinary Resources at www.heartwormsociety.org.

This American Heartworm Society guidance statement is based upon the cumulated knowledge and expertise of the American Heartworm Society's Board of Directors and AHS Scientific Committee experts, considering the latest information on heartworm disease, disease processes, known drug activity, and impact of these factors on disease management as of August 2011.

The American Heartworm Society needs your support. Please help us by becoming a member so that we can continue to provide information and guidance to the profession. Membership applications are available at www.heartwormsociety.org.

IMMITICIDE® is a registered trademark of Merial Limited, Duluth, GA.

©2011, American Heartworm Society. Use with acknowledgment of the American Heartworm Society.

REFERENCES

1. Dillon AR, Brawner WR, Hanrahan L. Influence of number of parasites and exercise on the severity of heartworm disease in dogs. In: Soll MD, Knight DH (eds): Proceedings of the Heartworm Symposium '95. Batavia, IL: American Heartworm Society, 1995, p 113.
2. Fukami N, Hagio M, Okano S, et al. Influence of exercise on recovery of dogs following heartworm adulticide treatment with melarsomine, Recent Advances in Heartworm Disease: Symposium '98. Batavia, IL: American Heartworm Society, 1998, pp 225-227.
3. Lok JB, Knight DH, LaPaugh DA, Zhang Y. Kinetics of microfilaremia suppression in *Dirofilaria immitis*-infected dogs during and after a prophylactic regimen of milbemycin oxime. Proceedings of the Heartworm Symposium '92. Batavia, IL: American Heartworm Society, 1992, pp 143-149.
4. Courtney CH, Zeng QY, et al. The effect of chronic administration of milbemycin oxime and ivermectin on microfilaremias in heartworm-infected dogs. Recent Advances in Heartworm Disease: Symposium '98. Batavia, IL: American Heartworm Society, 1998, pp 193-199.
5. Neer TM, Hoskins JD. Clinical experience with ivermectin used as a microfilaricide and for prophylaxis in the dog. Proceedings of the Heartworm Symposium '89. Batavia, IL: American Heartworm Society, 1989, pp 95-97.
6. Blagburn BL, Paul AJ, et al. Safety of moxidectin canine SR (Sustained Release) injectable in ivermectin-sensitive collies and in naturally infected mongrel dogs. Recent Advances in Heartworm Disease: Symposium '01. Batavia, IL: American Heartworm Society, 2001, pp 159-163.
7. Dzimianowski MT, McCall JW, et al. The safety of selamectin in heartworm infected dogs and its effect on adult worms and microfilariae. Recent Advances in Heartworm Disease: Symposium '01. Batavia, IL: American Heartworm Society, 2001.
8. McCall JW, Genchi C, Kramer L, et al. Heartworm and Wolbachia: Therapeutic implications Vet Parasitol. 2008;158:204-214 (Special issue: Heartworm Revisited - Selected papers presented at the 12th Triennial Heartworm Symposium 2007).
9. Bowman DD, Atkins CE. Heartworm biology, treatment, and control. Vet Clin North Am: Small Anim Pract. 2009;39(6):1127-1158.
10. Nelson CT, McCall JW, Rubin SB, et al. Diagnosis, Prevention, and Management of Heartworm (*Dirofilaria immitis*) Infection in Dogs (2010), accessed on 5 Aug, 2011 @ <http://heartwormsociety.org/veterinary-resources/canine-guidelines.html>.