Heartworm Disease 101
Updated September 2018

What is heartworm disease?

Heartworm disease is caused by a nematode parasite *Dirofilaria immitis*. This parasite is transmitted by mosquitoes, and makes its home in the pulmonary artery (blood vessel going from the heart to the lungs) and the right atrium (chamber of the heart). Mosquitoes are vital to transmission of heartworms, so heartworm disease tends to be more prevalent in areas of the country where mosquito populations are highest (i.e. southern US).

What Does Heartworm disease do to the body?

1.   Damage to the Pulmonary Arteries (the vessels going from the heart to the lungs):

Arteries do not do well having worms living inside them. The lining of the artery becomes damaged within days of the worm's arrival. Cells of the immune system are called into the area but the worm is far too big for these tiny cells to destroy. The resulting inflammation; however, continues to damage the artery. The arteries dilate and become tortuous (which may be visible on a radiograph). Aneurysms (ruptured vessels) and abnormal blood clotting (embolism) can result. Blood is shunted to other arteries that are not plugged up by worms and fluid begins to accumulate in the lung around the worm-filled arteries. Blood being sent to the lung is not efficiently oxygenated and areas of lung become consolidated and unable to participate in providing oxygen to the blood.

- Coughing and exercise intolerance result as areas of the lung are unable to participate in the blood oxygenation process.
- Nose bleeds may occur due to abnormal blood clotting in the lung.
- A form of non-infectious pneumonia (pulmonary eosinophilic granulomatosis) can result from excessive infiltration of inflammatory cells into the lung in response to the parasite.

2.   Heart Failure

Blood normally is pumped with ease through the arteries of the lung. With the arteries plugged with worms, the heart must pump harder against the pressure of the plugged arteries. This condition is called *pulmonary hypertension* and the right side of the heart must drastically increase its ability to work. It may be strong enough and it may not.

If worms begin backing up into the heart, there will be less space in the pumping chamber for blood to be pumped. The heart must pump through the high pressure system of the plugged arteries using less blood than normal. In order to meet the body's oxygen demand, the heart must pump faster and stronger still. There may come a point when the heart simply is not strong enough.

- When the heart muscle begins to thicken (as any over-worked muscle will), it may not conduct electrical impulses normally. This means that the pumping/filling rhythm can be disrupted and an *arrhythmia* may result.

In any heart disease, arrhythmia is a possibility; when arrhythmia is a possibility, so is sudden death.

- If the right side of the heart becomes too weak to keep up, fluid may accumulate in the chest cavity and abdominal cavity, leading to a pot-bellied appearance and/or difficulty breathing.

3.   Chronic Immune System Stimulation

When a dog goes without treatment for heartworm disease, their immune system becomes chronically stimulated. Antibodies, which are not only important tools of the immune system but are inflammatory proteins, are produced in high amounts all the time. These antibodies can cause a lot of trouble by precipitating in the delicate membranes of the eye, kidney, blood vessels, and joints. Antibodies can get stuck in these areas and damage these delicate membranes thus setting up tremendous tissue damage and pain.

4.   Caval Syndrome

Caval syndrome represents an especially disastrous form of heartworm disease. Here, there are so many worms (around 100) that the entire right side of the heart is filled with worms and they are backing out into the large veins that feed the right side of the heart. Usually there have been no signs of heart disease prior to the collapse, shock, and red blood cell destruction associated with this syndrome. Death usually occurs within 1 to 2 days and the only effective treatment is to open the dog's jugular vein and physically remove the worms with a special clamp. If enough worms can be removed to re-establish blood flow, the dog may survive.

Heartworm disease is a highly significant problem and must be managed both by dealing with the worms themselves and with the secondary issues they cause.

How is Heartworm Disease Treated?

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.

- **Class I: Lowest Risk**. Young healthy dogs with minimal disease evident on x-ray, normal blood work, and no symptoms of illness. They may cough only occasionally if ever, they only fatigue with exercise, and their chest x-rays are normal.
- **Class II: Moderately Affected**. Healthy dogs with minimal signs as above, occasional coughing, fatigue only with exercise but with chest x-rays that show definite evidence of heart disease. Lab testing may show mild anemia, urine tests show some protein, but not severe urine protein loss.
- **Class III: Severely Affected**. Dog is suffering from weight loss, cough, difficulty breathing, blatant damage to the vasculature is apparent on chest x-rays, 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 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.

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

- The microfilaria (early larval stages – L1), 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 microfilaria that can spread to other dogs through a mosquito, where the develop into the early larval stages. The microfilarias are killed with regular monthly heartworm preventatives.

- The new arrival heartworm larvae, delivered from mosquito bites in the last 6 to 7 months. These are L3 and L4 larvae stages. These will continue their maturation and repopulate the heart and pulmonary arteries if they are not killed before the treatment of 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.
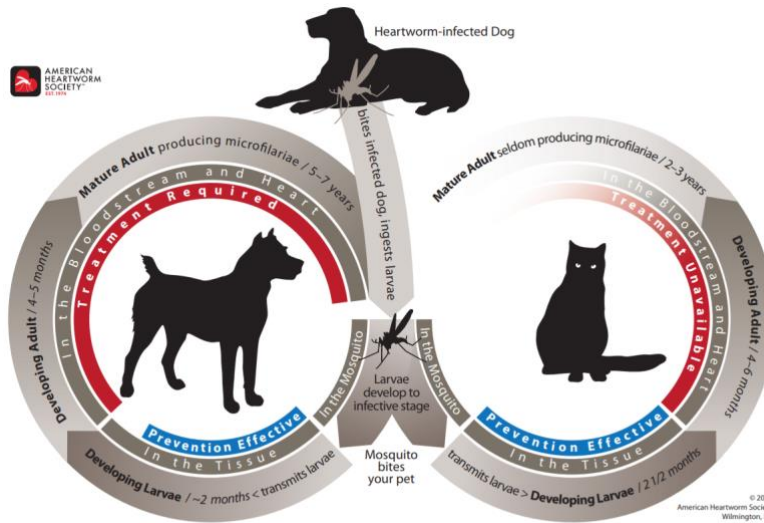
The first step in treatment is clearing the migrating immature worms. If we were to jump directly to killing the adult worms first, the adult worms we remove could be readily replaced shortly afterwards by those that were in the process of migration at the time of treatment. By addressing the migrating immature worms first, we minimize the number of adult worms we must kill in the second step. Fewer adult worms dying at once also means less risk.

The L3 and L4 larvae can all be killed by monthly ivermectin-based heartworm preventive products (i.e. Heartgard, Tri-Heart, etc.). There are other products that can kill these stages, but often much faster, which can create circulatory shock if there are large numbers of microfilariae dying all at one time. The American Heartworm Society recommends at least 2 months of a preventive prior to treating the adult worms.

The only product currently available for the treatment of adult heartworms is melarsomine dihydrochloride (Diroban by Zoetis and 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 and The American Heartworm Society, however, recommend treating all patients with the three-dose protocol as it creates a more gradual kill of the adult worms, which is safer as it reduces the risk of embolism and shock and may have a slightly higher success rate. However, in a rescue setting, due to the often low worm burden of affected dogs, their asymptomatic nature, and the difficulty of keeping them quiet for the two month treatment period, the "single" protocol is often elected, in which two injections are given over a 24 hour period (versus one injection followed a month later by two injections 24 hours apart).

The patient receives an intramuscular injection deep in the lower back muscles. As this injection induces inflammation at the site, there is often some degree of discomfort associated with this in the days after treatment. Therefore, pain relieving medication is often prescribed for several days post-injection. A small percentage of dogs experience some sort of reaction at the injection (soreness, swelling, etc...) site that resolves in 1 to 4 weeks. Some dogs develop a permanent firm lump at the site of injection.

Day	Treatment	
	"Single" (two-injection) protocol	**"Split" (three-injection) protocol**
Day 0	Dog diagnosed and verified as heartworm positive: ● Positive antigen (Ag) test verified with microfilaria (MF) test ● If no microfilariae are detected, confirm with 2nd Ag test from a different manufacturer Begin exercise restriction. The more pronounced the signs, the stricter the exercise restriction If the dog is symptomatic: ● Stabilize with appropriate therapy and nursing care ● Prednisone prescribed at 0.5 mg/kg BID 1st week, 0.5 mg/kg SID 2nd week, 0.5 mg/kg EOD 3rd and 4th weeks	
Day 1	Administer heartworm preventive. ● If microfilariae are detected, pretreat with antihistamine and glucocorticosteroid, if not already on prednisone, to reduce risk of anaphylaxis ● Observe for at least 8 hours for signs of reaction	
Days 1-28	Administer doxycycline 10 mg/kg BID for 4 weeks. ● Reduces pathology associated with dead heartworms ● Disrupts heartworm transmission	
Day 30	Administer heartworm preventative	
Day 60	Administer heartworm preventive. First melarsomine injection 2.5 mg/kg intramuscularly (IM) Prescribe prednisone 0.5 mg/kg BID 1st week, 0.5 mg/kg SID 2nd week, 0.5 mg/kg EOD 3rd and 4th weeks. Decrease activity level even further. ● Cage restriction/on leash when using yard	Administer heartworm preventive. First melarsomine injection 2.5 mg/kg intramuscularly (IM) Prescribe prednisone 0.5 mg/kg BID 1st week, 0.5 mg/kg SID 2nd week, 0.5 mg/kg EOD 3rd and 4th weeks. Decrease activity level even further. ● Cage restriction/on leash when using yard
Day 61	Second melarosamine injection 2.5mg/kg IM	
Day 90	Administer heartworm preventive.	Administer heartworm preventative. Second melarsomine injection 2.5 mg/kg IM
Day 91	Administer heartworm preventative.	Third melarsomine injection 2.5 mg/kg IM Prescribe prednisone 0.5 mg/kg BID 1st week, 0.5 mg/kg SID 2nd week, 0.5 mg/kg EOD 3rd and 4th weeks. Continue exercise restriction for 6 to 8 weeks following last melarsomine injections.
Day 120	Establish year-round heartworm prevention.	
Day ~240	Antigen test 9 months after completion; screen for microfilariae.	
Day ~270		Antigen test 9 months after completion; screen for microfilariae.

An option that has been posed to treat heartworm disease is a "slow-kill method" - to simply leave the dog on an ivermectin-based preventive. This is not ideal for the dog as the heartworm disease is still progressing during this time. This approach is typically only considered in dogs with significant underlying disease that may be exacerbated by the treatment or worm die-off (primarily kidney disease).

Management of a Dog Before & After Adult Heartworm Treatment

From the time of diagnosis to adult heartworm treatment, it is important to start to implement exercise restrictions. This is for two reasons:
1. These dogs have compromised heart and lungs...they are at increased risk of developing inflammation of the lungs, throwing blood clots, etc...
2. They will need to be STRICTLY exercised restricted/crate confined for at least one full month after treatment so it's best to get them adjusted to this ahead of time.

After treatment, the patient must be strictly confined for one month following the final treatment. No walks greater than 5 minutes, no running around, no jumping or playing. Ideally these dogs are crate confined or confined to a small area of the house, and they go out on leash to urinate and defecate. The reason for this is that embolism (clots to the lungs) is to some degree an inevitable consequence of successful adult heartworm treatment and may be severe if infection is heavy and pulmonary arterial disease is extensive. It is important to minimize embolism-related problems: exercise increases heart rate and oxygen demand, so we aim to keep the heart rate and blood pressure normal during the recovery period. If signs of embolism (low grade fever, cough, bloody nose, exacerbation of right heart failure) develop, they are usually evident within 7 to 10 days, but occasionally as late as 4 weeks after completion of adult heartworm treatment. Mild embolism in relatively healthy areas of lung may be clinically inapparent. **A pivotal factor in reducing the risk of complications is STRICT exercise restriction.**

Monitor for:

- Coughing
- Inappetence
- Lethargy
- 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 month following treatment, and even prior to treatment in rare cases.

Lu's Labs recommends taking a heartworm antigen test on all heartworm negative dogs as per the contract date, nine months after 1 shots for dogs that went through the treatment and puppies between 8-9 months of age in order to ensure any previously undetectable infections are diagnosed as early as possible.