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Feline Heartworm Disease: Fact or Fiction?

The mosquito-borne parasite *Dirofilaria immitis* is known to infect multiple species, including dogs, cats, ferrets, wolves, coyotes, foxes, sea lions, and even humans.¹ Canids, including dogs, are the definitive hosts, while cats are viewed as aberrant or atypical hosts.¹ Unlike dogs, in North and South America, *D immitis* is the only filarial disease that infects cats.²

Heartworm disease was first reported in cats in Brazil in 1921, yet some still believe that cats cannot be infected with *D immitis*.² A 2007 study demonstrated that when dogs that were not administered a heartworm preventive were artificially infected with 100 L3 larvae, approximately 75% of the larvae developed into adult heartworms in every dog. When cats that were not administered heartworm preventive were artificially infected with 100 L3 larvae, 3 to 10 adult worms were found in 75% of the cats.² This study demonstrated that cats can be successfully infected with heartworms.²

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The 2007 study also demonstrated that the rate of infection and development of infective heartworm larvae into adults in cats is significantly lower than that of dogs in the same geographic area.² Studies conducted in the 1990s found that about 2.5% to 14% of cats in the southeastern United States were infected with heartworms—numbers similar to or higher than FeLV or FIV infection rates.³ A study conducted at North Carolina State University showed that 25% of the infected cats there were considered by their owners to be strictly indoor cats,³ indicating that living indoors does not provide adequate protection from mosquito bites.

In 2001, the American Heartworm Society reported more than 244,000 positive heartworm tests for dogs and 3,000 positive tests for cats. Considering the problems with testing in cats, as well as the low number of tests performed, this report is assumed to underrepresent the true incidence of the disease. The nationwide incidence in cats is estimated to be approximately 12%.³

The reliability of heartworm testing, which depends on the presence of heartworm antigen or microfilariae, is affected by the relative lack of both in cats. Because cats are aberrant hosts, the lifespan of adult heartworms is reduced in this species, resulting in a shortened period of patency. As a result, microfilariae, produced by adult female heartworms in the presence of adult male heartworms, are uncommon in cats. It is believed that some cats may be able to spontaneously rid themselves of an infection with a strong immune response.⁴

DISEASE PHASES

If cats are able to spontaneously rid themselves of adult heartworms, should patent infections be of concern?

Heartworm disease in cats can have 2 active phases. As in dogs, surviving L3 larvae molt to the L4 stage and migrate through body tissues. The immature worms arrive in the lungs between 60 and 100 days after the infected

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bite, initiating a severe inflammatory response. In cats, this response, the first active phase, has been called *heartworm-associated respiratory disease*, or *HARD*, and it is responsible for the pathology seen in the arteries of the lungs as well as the bronchioles and alveoli.^{1,4} If any immature worms survive this immunologic onslaught and make it to adulthood, the initial inflammatory response may recede.

Phase 2 is initiated when the adult worms begin to die. In dogs, adult worms can live in the heart and lungs for more than 5 years, but in cats, the typical lifespan is less than 2 years.² The release of new heartworm debris into the bloodstream initiates a second inflammatory response, also primarily localized in the lungs.⁴ Lesions in the second phase of infection are associated with dead worm fragments as the immune system removes them from the body. The only exit for parasitic debris in the bloodstream is through the action of phagocytic cells.

IMMUNOLOGIC RESPONSE

The severe inflammatory response to the arrival of the immature worms in the pulmonary arteries prompts the mobilization of pulmonary macrophages, which are designed to envelop and digest foreign material such as bacteria and parasites. Macrophages that behave in this manner in response to a dirofilarial infection are not present in dogs, explaining the

difference in response in cats. However, while the feline immune system attacks the arriving worms, evidence suggests that the worms are able to suppress the immune response.²

The special macrophages are also key players in the intense inflammatory reaction to the debris created when adult heartworms die, leading to pulmonary dysfunction and HARD. This round of immunologic responses can occur with each infected bite, as well as with death of each adult worm.^{2,4}

The death of immature heartworms in the lungs of cats may cause severe pulmonary clinical signs similar to those seen with feline asthma. These signs may appear as early as 80 to 90 days after infection, a full 3 months before adult female heartworms would begin to release antigen into the bloodstream. Because commonly used canine heartworm antigen tests identify this antigen, these tests cannot be used to confirm a diagnosis of heartworm disease during the initial disease process in cats. To further complicate diagnosis, accompanying pulmonary radiographic lesions are not specific for heartworm disease and could represent true feline asthma or other parasitic infections such as visceral larval migrans. Because of their small size (microfilariae require 40× to 100× magnification to be seen on microscopy), worms and worm fragments cannot be seen using readily available imaging techniques.²

LUNG CHANGES

In addition to the inflammatory response, immature heartworms can cause embolization of pulmonary arteries. With embolization of these vessels, gas exchange is compromised or absent. Obstruction of blood flow through the lungs, especially in the caudal pulmonary arteries, causes acute respiratory signs, and the involved lung lobe becomes hemorrhagic, with local areas of edema. Signs of inflammation can be seen in lung lobes not associated with the embolization, indicating that the disease is not simply an obstructive disease (**FIGURE 1**). Immature worms arriving in the pulmonary vasculature can cause pulmonary arterial,

arteriolar, and airway lesions as severe as those seen with death of adult heartworms.

If the cat survives the initial embolic event, recanalization around the obstruction occurs rapidly, and lung function is markedly improved within days. Median survival is 1.5 years for all infected cats and 4 years for those that survive their first 24 hours after this severe respiratory episode.³

In chronically infected cats, perivascular reactions and evidence of thrombus formation can be seen, but cardiac changes are minimal compared to those seen in dogs.² In cats, acute lung injury caused by the death of adult worms can result in generalized respiratory failure. A significant acute inflammatory component can be seen, especially when the adult heartworms die.²

CLINICAL SIGNS AND PHYSICAL EXAMINATION FINDINGS

The inflammatory response to the arrival of immature worms in the lungs may cause asthma-like signs.² These cats may initially present with a history of coughing, dyspnea, and vomiting. Rapid and difficult breathing may be noted on examination. Additionally, the owners may note lethargy, anorexia, and weight loss. Alone, none of these signs



FIGURE 1. Lung from cat with heartworm-associated respiratory disease but no adult heartworm. Signs of inflammation include red color and rounded margins. Healthy lungs are pink with sharp margins. Image used courtesy of Zoetis

is diagnostic for heartworm infection.^{2,4} Coughing is usually temporary and is initially responsive to corticosteroids.

Physical examination findings are usually within normal limits, but there may be a systolic murmur over the tricuspid valve area, and occasionally a gallop rhythm is noted. Uncommonly, harsh lung sounds may be heard; these are often referred to as *dry rales*.²

Clinical signs and, possibly, thoracic radiographic findings are similar in cats with abbreviated heartworm infections and those with other causes of bronchial disease, such as feline asthma. An abbreviated infection can be caused by spontaneous removal of the larvae by the cat's immune system or treatment with a preventive drug such as ivermectin or selamectin. Because of this, it is possible that HARD is underdiagnosed, particularly in geographic areas where heartworm infections are common.⁴

Unfortunately, one of the primary signs of adult heartworm death in cats is sudden death of the host.² This has been attributed to circulatory collapse and respiratory failure from acute pulmonary arterial infarction and acute lung injury.² Acute respiratory collapse may occur with or without previous clinical signs.

DIAGNOSTICS

Diagnostics can be a challenge in a dyspneic cat, involving a complete physical examination, thoracic radiography, cardiac ultrasonography, angiocardiology, a complete blood count, heartworm antigen/antibody tests, and microfilaria testing.¹ The specificity and sensitivity of these tests vary, and there is no one ideal test for heartworm disease in cats. Necropsy may be required in cases of sudden death.¹

Radiography

Even though the pulmonary parenchymal changes are nonspecific and can change rapidly in infected cats, thoracic radiography has proven to be a valuable diagnostic tool for heartworm disease and has the

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advantage of being available for most practitioners. Lung changes can include diffuse or coalescing infiltrates, perivascular densities, and lung atelectasis. On radiographs, enlarged pulmonary arteries are evident, with ill-defined margins. Changes are usually most prominent in the lower (caudal) lobes of the lungs (**FIGURE 2**).¹

Ultrasonography

Unlike in dogs, adult worms are seldom found in the heart in cats (**FIGURE 3**). Cardiac ultrasonography of adult worms in the main pulmonary artery and close portions of the right and left branches of the artery enable definitive diagnosis of heartworm disease. Parallel hyperechoic lines representing an image from the adult heartworm's cuticle (outside



FIGURE 2. The most common radiographic findings in feline heartworm disease are enlargement of the right caudal lobar artery and a bronchointerstitial inflammatory pattern in the caudal lung lobes.³ Image used courtesy of Zoetis

lining) are consistent with the presence of adult heartworms.² With ultrasonography, it is virtually impossible to visualize the smaller pulmonary arteries where young worms are often found.¹ The ability to find heartworms with ultrasonography depends on the cooperation of the patient, the skill of the ultrasonographer, and the location of the worms.

Antigen Testing

Unlike radiography and ultrasonography, which do not depend on the sex of the heartworm(s), antigen testing is most accurate at detecting infection with 1 or more female worms that are at least 7 to 8 months old (sexually mature). The specific antigen detected during testing is produced by the gravid adult female worm's uterus. Antigen testing is not as effective at detecting infection with adult worms <5 months old and is unable to detect immature worm infections, male-only infections, and some infections with only one adult female worm.¹ If the infection does not produce an adult worm, the worms are immature at the time of testing, or only male adult worms are present, a false-negative result may be obtained. Therefore, a positive antigen test is diagnostic for active adult heartworm infection, but a negative antigen test does not rule out infection. Most cats with heartworm disease are antigen negative because of low titers.²



FIGURE 3. Adult *Dirofilaria immitis* in a feline heart. In cats, usually only 1 to 3 adults are found. Image used courtesy of Zoetis

ELISA Testing

Antibody testing uses an enzyme-linked immunosorbent assay (ELISA) that detects feline antibodies to heartworm antigen. These antibodies are produced in response to early migration of L3 and L4 larvae. Positive results can be detected 2 to 3 months after infection. Initial studies of cats that have naturally eliminated the adults or microfilariae show that the host antibody gradually decreases to negative concentrations after 4 to 6 months.

Cats that are on a macrolide preventative (ie, selamectin, ivermectin, or moxidectin) can have a false-positive ELISA result after being bitten by an infected mosquito, with resultant larvae death and no persistent infection.² Because antibodies are produced after the initial exposure, a positive result indicates that the cat has been bitten by a *D immitis*-carrying mosquito 2 to 3 months previously, but not whether it is currently infected. Use of purified recombinant heartworm antigen can increase test sensitivity for an active infection.¹

The ELISA is a method of analysis, and variations in antigen preparation, antibody sources, and laboratory techniques between diagnostic labs and in-house testing kits can create variation in results.² The death of adult heartworms and subsequent release of large amounts of antigen from decomposing fragments may produce a strong antibody response. Some of the highest titers are associated with severe clinical signs in cats after adult worms have died and the disease itself may be resolving.²

Immunofluorescence Assay Testing

An immunofluorescence assay (IFA) can be used to detect cuticular antigen expressed by adult heartworms. IFAs detect approximately 33% of positive infections. They are not effective in detecting infections with immature worms, sterile worms, single-sex infections, or absence of a host response.² Somatic IFAs, which look for antibodies to microfilarial somatic antigen, are nonspecific. IFAs have been helpful in researching the biology of parasite–host interaction but have demonstrated limited application in clinical diagnostics.²

Blood Testing

A complete blood count may show a mild anemia (hematocrit 23%–33%) in 30% of cases, with nucleated red blood cells and rare basophils present. Approximately 30% of infected cats have elevated eosinophil counts, although this depends on the phase of the disease when the cat is tested (FIGURE 4). During the initial inflammatory phase and when adult worms are dying, the eosinophil count can be higher than during the state between these 2 phases of infection.²

Electrocardiography

Electrocardiography can be useful in detecting the subtle sign of right ventricular enlargement. Ectopic ventricular beats and other arrhythmias are occasionally seen after adulticide treatment in asymptomatic cats.² As neither of these findings is consistent with heartworm disease, this diagnostic test is likely of little value alone.

Cytology

Tracheal cytology may be performed on a cat that is sedated rather than under full anesthesia. The presence of eosinophils in the recovered tracheal fluid is consistent with heartworm disease, feline asthma, and parasitic lung disease. In heartworm disease, eosinophils can be found in the recovered fluid

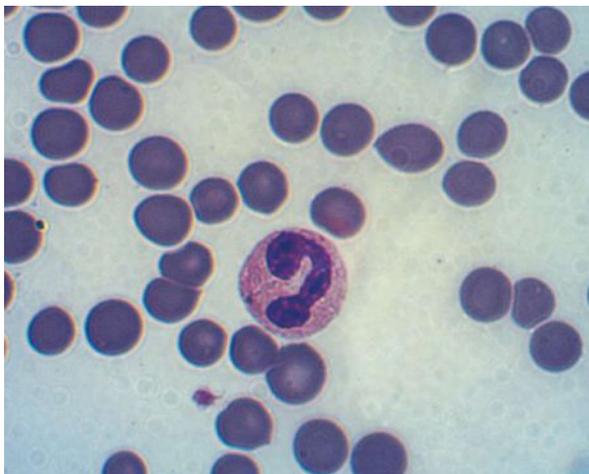


FIGURE 4. Feline eosinophil. The presence of eosinophils is consistent with a parasitic or allergic infection but is not specific for either. Image used courtesy of Zoetis

4 to 7 months after L3 infection; however, they may not be present later in the infection even if adult worms are present. Tracheal cytology consistent with chronic inflammation may be present after eosinophilia has resolved.²

Bronchoalveolar lavage can be performed if the cat is stable enough to be placed under anesthesia. Eosinophils may or may not be present in the lavage fluid, but the presence of basophils is highly suggestive of heartworm disease.² Lavage is highly unlikely to retrieve larvae or adult worms, as these parasites are located within the pulmonary vessels and not within the bronchioles and alveoli.

Necropsy

On necropsy, the general pulmonary pathology of infected cats is similar to that of infected dogs: muscular hypertrophy of the main vessels of the lungs, villous endarteritis, and cellular infiltrates of the adventitia (the outmost layer of the blood vessels; FIGURE 5).² Obviously, finding adult worms or fragments would be consistent with death due to lung collapse related to worm death.

TREATMENT

Adulticide Therapy

No approved treatment for feline heartworm infection currently exists. While adulticide thiacetarsamide treatment is well tolerated by cats without immediate complications, the

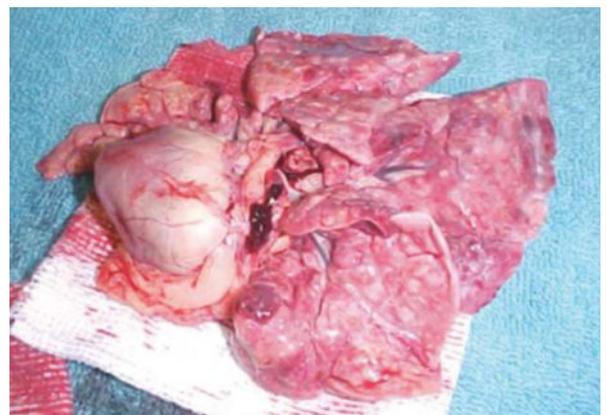


FIGURE 5. Feline lungs showing consolidation and inflammation caused by heartworm-associated respiratory disease. Image used courtesy of Zoetis

arrival of dead worms and worm fragments in the pulmonary vasculature causes an immunologic response that results in significant pulmonary edema within 2 days of the initial injection. Death as a result of respiratory collapse may ensue. Pulmonary edema may be responsive to oxygen therapy and high-dose corticosteroid treatment.² The routine use of corticosteroids is not recommended before or after thiacetarsamide treatment, and aspirin is contraindicated in feline heartworm disease.

Sudden death due to embolization can occur after adulticide treatment, especially within the first 10 days after administration. Embolization can also induce severe lung injury, hemoptysis, and dyspnea.

The advantage to treating a cat with an adulticide is being able to observe it during the 2-week period after treatment while the worms are dying, compared to not knowing when the heartworms will die naturally in an untreated cat.²

Immature larvae are thought to be resistant to thiacetarsamide, meaning that any developing heartworm larvae present at the time of treatment will not be killed. If any of these larvae subsequently develop into adult worms, the cat may have a second adult infection.²

Ivermectin treatment is successful in removal of microfilariae, but does not kill adult worms, although the remaining female worms may become sterile. Canine doses of Immiticide should not be used in cats.²

Conservative Therapy

In light of the significant risks associated with adulticide treatment, many owners opt for conservative therapy for heartworm-infected cats. This does not eliminate the chance of embolization, but it can help manage the signs of respiratory distress and dyspnea. Alternate-day prednisolone therapy has been successfully used to help manage clinical signs of coughing and vomiting. It has no effect on progression of lesions in the lungs, as evidenced by radiography.² An emergency dose of an oral or injectable glucocorticoid should be given to the owner in the event of a severe episode of

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collapse or dyspnea, to allow them time to get the cat to an emergency facility for additional treatment. As this therapy addresses only the inflammatory response, not the vascular trauma or the presence of migrating larvae or surviving adults, the chance of acute death is still present.

In the event of respiratory distress or collapse, emergency treatment involving oxygen therapy, cage rest, small volumes of IV fluids, and injectable prednisolone can result in clinical improvement and resolution of clinical signs within 24 hours.

PREVENTION

Feline heartworm disease is challenging to diagnose and has no approved, effective, or safe treatment, but highly effective preventives are available: Heartgard (merial.com), containing the active ingredient ivermectin, Revolution (zoetis.com), containing the active ingredient selamectin, and Advantage Multi (bayerdvm.com), containing the active ingredient moxidectin, are all approved for prevention of heartworm in cats. Heartgard is available as an oral chew and is administered once monthly. Revolution and Advantage Multi are topical medications that are applied to the skin, also once monthly.

Both ivermectin and selamectin can be given to kittens as young as 6 weeks of age and continued for the life of the cat. Moxidectin should not be applied to kittens younger than 9 weeks of age. Because mosquitoes can be found indoors,

current recommendations are to administer these medications year-round in endemic areas.

Since current antigen testing is inconsistent in cats, especially those with low worm counts, it is not recommended to test asymptomatic adult cats before administering preventive therapy. For cats with subclinical signs of heartworm infection, progression to obvious signs of allergic lung disease can be seen after preventive administration. Despite this, heartworm-positive cats can be safely placed on preventive medications, which will help prevent another round of infection.

CONCLUSION

In areas where dogs are exposed to mosquitoes that carry *D immitis*, so are cats. Although heartworm disease in cats can be self-limiting, with a small number of cats able to spontaneously rid themselves of adult worms, migrating larvae damage

the lungs and vasculature before clinical signs appear. In some cats, the first sign of infection is acute respiratory collapse and death, which can be devastating to owners.

Even if you do not see heartworm-positive cats in your practice, rest assured that they are seeing you every week. Fortunately, effective preventives exist. By educating clients about the facts of HARD, veterinary technicians can help improve feline health! ■

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