1999 Guidelines for the Diagnosis, Treatment, and Prevention of Heartworm (Dirofilaria immitis) Infection in Cats

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PREAMBLE
Since the Council published its first set of guidelines in 1995, feline heartworm disease (FHD) has been given considerable attention in veterinary professional publications and in press releases. As a result of this heightened general awareness, heartworm infection in cats is being diagnosed more frequently, thereby providing further tangible evidence of its potential importance. In response to the demonstrable need for better diagnostic tests and means of protecting cats at risk of infection, new products have been developed to specifically address these demands. However, as more experience with this disease has been gained, new issues have arisen. These revised guidelines for the diagnosis, treatment, and prevention of FHD build upon the previous conceptual foundation, and based on the latest available information, provide a consensus opinion of how best to deal with this disease.
There are significant differences between FHD and its classical canine counterpart, and these are consistent with characteristics of partially adapted host-parasite relationships. Although cats are a susceptible host, they are more resistant to infection than are dogs. Most heartworm infections in cats are comparatively light and consist of less than six adult worms. Although much heavier infections occur occasionally, usually only one or two worms are present and approximately one third of these consist of same sex worms. Because of their relatively small body size, cats with only a few worms are still considered to be heavily infected in terms of parasite biomass. Some clinical surveys and data from experimentally-infected cats have documented a slight preponderance of infection in male cats, but it has not been determined conclusively that male cats are at greater risk. No sex predilection for anti-Dirofilaria immitis host antibody seropositivity has been proven within populations of naturally exposed cats, nor has a preference by vector mosquitoes for either sex; although, some data suggest trends for each toward female cats. However, host preference by some of the most abundant vectors does favor the dog and may contribute to the lower prevalence of infection in cats. Also, the true prevalence of heartworm infection in cats is probably understated due to diagnostic limitations, and the greater tendency of cats to exhibit only transient clinical signs or die without confirmation of infection. Circulating microfilariae (MF) are seldom found in infected cats. When microfilaremias do develop in cats, they occur slightly later (195 days postinfection at the earliest) than in dogs and seldom persist beyond 228 days (7.5 months) postinfection. Since heartworms transplanted from cats are capable of resuming production of circulating MF in dogs, it appears feline infections become occult due to host immune-mediated clearance of the MF and perhaps a reversible suppression of MF production.

There are other indications that the cat is an imperfect host for heartworms. Aberrant migration occurs more frequently in cats than in dogs. Though uncommon, ectopic heartworms are found disproportionately often in the body cavities, systemic arteries, and central nervous system of cats. Also, in cats, the parasite has a shorter life span, which is thought to be two to three years. Despite this, heartworms are capable of causing severe disease in the cat.

The clinical importance of heartworms is amplified in cats because even a small number of heartworms is potentially life-threatening. Though live adult worms in the pulmonary arteries cause a local arteritis, some cats never manifest clinical signs. When signs are evident, they usually develop during two stages of the disease. The first coincides with the arrival of immature adult (fifth stage) worms in the pulmonary arteries four to six months postinfection. These early signs appear to be induced by an acute vascular and parenchymal inflammatory response triggered by activation of pulmonary intravascular macrophages, which are plentiful in cats but not dogs. If not fatal, this acute phase subsides. Many cats tolerate their infection without apparent ill effects until the mature worms begin to die and the degenerating parasites cause pulmonary inflammation and thromboembolism. In dogs, the caval syndrome (dirofilarial hemoglobinuria) results partly from large numbers of heartworms interfering with closure of the tricuspid valve. Caval syndrome occurs rarely in cats because usually they are infected lightly and do not have worms in the valve orifice. However, even one or two worms may cause tricuspid regurgitation and a heart murmur.
Arterial intimal proliferation resembling the characteristic heartworm arteritis found in dogs also develops in the major lobar and peripheral pulmonary arteries of cats. Since heartworm infections in cats usually are light, and of relatively short duration, these lesions are localized and ordinarily fail to cause sufficient obstruction to produce clinically significant pulmonary hypertension. Consequently, right ventricular hypertrophy and right heart failure are infrequent complications. Even when narrowing of a lumen is compounded by thrombosis at the nidus of embolic worm fragments, the bronchopulmonary collateral circulation usually is adequate to prevent infarction of the lung.

Heartworm infected cats, like dogs, may develop interstitial lung disease. However, in cats there also may be extensive hyperplasia of the surfactant producing type two cells in the alveolar walls. These parenchymal lesions may have an important role in the pathogenesis of the acute respiratory distress that many cats experience four to nine months postinfection. These attacks are frequently misdiagnosed as asthma. Some cats go into remission and eventually recover.

However, sudden death, nearly always associated with degenerating worms in the pulmonary arteries, and severe lung congestion can occur.

**PHYSICAL DIAGNOSIS**

**Clinical Signs and Physical Findings**

Many cats tolerate their infection without displaying clinical signs and frequently, those signs that manifest transiently are too nonspecific to initially suggest heartworms as the cause. Clinical signs associated with FHD may be only a vague malaise or can comprise predominantly respiratory, gastrointestinal, ie, emesis, or occasionally neurologic manifestations, expressed in either an acute or more often, a chronic presentation. Signs of chronic respiratory disease, such as persistent tachypnea, intermittent coughing, and increased respiratory effort are most common. A systolic heart murmur may be present in cats with worms in the right atrium and ventricle. Anorexia and weight loss occur in some cats. Intermittent vomiting unrelated to eating is reported frequently and if no obvious cause seems evident, this should raise suspicion of heartworm infection. Serous effusion in the chest and abdomen, ataxia, and syncope occur but are uncommon. Heartworm infection also has been reported in some cats with respiratory distress due to chylo or pneumothorax. A peracute syndrome consisting of respiratory distress, ataxia, collapse, seizures, hemoptyysis, and sometimes sudden death, occurring singly or in some combination, may arise without warning.

**DIAGNOSTIC TESTING**

Heartworm infection in cats is a more elusive diagnosis than in dogs and can be overlooked easily. A conscious awareness of its existence is critical, as is a willingness to pursue a high index of suspicion based on historical and physical findings. This frequently entails application of multiple diagnostic tests, some of which may need to be repeated on several occasions. Of these, heartworm serology, thoracic radiography, and echocardiography are the most useful methods of clinical confirmation.

**Microfilariae**

Cats are seldom microfilaremic when examined. In the Americas, only *D. immitis* microfilariae have been identified but in northern Italy, microfilariae of *Dirofilaria repens* also have been found in cats. Since few microfilariae are ever present, the chances of finding them are improved by using the modified Knott or millipore filter concentration techniques.
Serology

Since first publishing these guidelines three years ago, considerable additional experience has been gained testing for host anti-
D. immitis antibody and circulating adult female heartworm-derived antigen. Every combination of antibody and antigen test results has been seen and it is now recognized that their interpretation is more complicated than originally appreciated. Consequently, our understanding of the utility and limitations of heartworm serodiagnosis in cats continues to evolve.

Statistically significant seroepidemiologic data for cats only now are accumulating. Based on the low prevalence of antigenemic cats, antigen tests have been considered too insensitive to reliably diagnose infection. Three factors primarily account for the perceived lower reliability of antigen tests in cats than in dogs. Unisex infections are more common in cats and none of the presently available antigen tests can be relied upon to detect infections by only male heartworms. Secondly, feline infections usually are light and there may be insufficient numbers of mature female worms to produce a detectable antigenemia. Thirdly, some cats may become ill before a detectable antigenemia develops at about 5.5 to eight months postinfection. Consequently, antibody testing, which for lack of specificity was superceded when the more accurate antigen tests became available for the dog, has regained favor for use in cats, on the strength of its greater sensitivity. The principal advantage of antibody testing is greater sensitivity due to the fact that larvae of either sex can stimulate a detectable host immune response as early as two months postinfection. Also, the specificity of current cat antibody tests is higher than the comparatively crude prototypes developed previously for testing dogs. The more strongly positive an antibody test result, the greater the probability that there has been exposure to at least the late fourth larval stage, if not adult heartworms. In conjunction with other provocative findings, antibody seropositivity may be pivotal in making a clinical diagnosis of FHD.

Antibody testing has been conducted largely among populations of cats in which the rationale for testing individual members frequently has not been well defined. Since the composition of the largest databases reflects some bias toward heartworm suspects rather than random selection, seroprevalence statistics are skewed somewhat toward infected cats and probably over estimate the actual frequency of heartworm infection in regional populations. Since at this time, heartworm chemoprophylaxis has not been administered widely to cats, its limited use has not yet confounded significantly the existing epidemiologic data. Given these caveats, approximately 15% of tested cats, on average (>30% in some regions), develop antibody to heartworms, but only about 5% of these (~0.75% of the entire test population) also are antigen positive. Although antigenemia under represents the actual number of mature infections, the infrequency of heartworm antigenemia is consistent with the relatively low number of cats with confirmed FHD. However, with the advent of antibody testing, it is apparent that the combined prevalence of transient larval and mature adult infections is considerably higher than previously recognized.

It is evident that correctly interpreting antibody test results requires additional information and thoughtful analysis. However, when infection with adult female worms actually exists, antigen tests are more reliable than generally credited. Agreement between different antigen tests (canine tests approved for use in cats as well as feline proprietary tests) is very high, but considerable disparity exists between the results of antibody tests utilizing whole worm extracts and those utilizing recombinant antigen probes. The earlier detection and ap-
parent greater sensitivity of whole worm extract antibody tests in experimentally-infected cats does not make them superior tests per se since that early in the life cycle, it is problematic whether the parasite will survive to eventually cause clinical disease. Greater sensitivity per se of one antibody test over another is not necessarily an asset when infection status is unknown since a positive test may only reflect exposure to larvae that may not complete development or cause clinical disease. A positive antibody test in a cat displaying signs suggestive of FHD is not conclusive evidence of concurrent active infection or FHD and must be viewed in the context of additional correlative findings in order to distinguish between mere coincidence and cause. In this regard, quantification of the antibody response expressed in antibody units or by titer, and serial monitoring may be necessary. The more antibody, the greater the likelihood that a clinically significant infection exists. Many cats are only transiently antibody positive and conversion to negative (and vis versa) of either antibody or antigen can be critical in properly interpreting the patient’s heartworm status.

Table 1 illustrates the complementary nature and possible interpretations of combined antibody and antigen test results.

The high specificity of heartworm antigen tests makes antigen detection nearly certain confirmation of concurrent or recent infection with adult worms. However, based on antibody testing, the distinction between sensitization to self-limiting larval migration and infection with adult worms is less clear. Results of both tests should be carefully considered in reference to other correlative evidence of FHD before rendering an interpretation.

**Thoracic Radiography**

Independent of serologic test results, radiography may provide strong evidence of FHD, and is valuable for assessing the severity of disease and monitoring its progression or regression. The most characteristic radiographic features of heartworm disease in cats, as in dogs, are a sometimes subtle enlargement of the main lobar and peripheral pulmonary arteries, characterized by loss of taper, and sometimes tortuosity and truncation in the caudal lobar branches. These vascular features are visualized.
best in the dorsoventral view and may be visible only in the right caudal lobar artery where heartworms are found most often. The characteristic morphology of the pulmonary arteries in infected cats, unlike dogs, tends to normalize and may disappear completely, leaving no residual evidence of infection. Enlargement of the main pulmonary artery segment may occur in heavily infected cats but is not a hallmark feature since it is obscured by the cardiac silhouette. The cardiac silhouette itself is seldom enlarged. A bronchointerstitial lung pattern that may clear spontaneously within a few months is a common secondary feature, suggestive of but not unique to FHD. Other less commonly associated pulmonary findings include hyperinflation of the lungs with flattening of the diaphragm, focal parenchymal radiodensities, consolidated lung lobes, pleural effusion, and pneumothorax. In some cases of FHD, thoracic radiographs provide no evidence of infection.

Radiographic features suggestive of FHD can be found in about half of the cats suspected of being infected, based on physical signs. Also, about half of those cats with pulmonary arterial enlargement indicative of FHD are antibody positive. The probability of finding enlarged pulmonary arteries is even greater among cats that are antigen positive. Temporal differences in the development of the parasite, host immune responses and organic disease may account for discrepancies between radiographic, clinical and serologic findings.

Angiography

This is the most vivid method of delineating the characteristic morphologic deformation of the pulmonary arterial vascular tree caused by heartworm infection. Sometimes heartworms also may be visualized as linear filling defects within opacified branches. However, since serologic testing has become routine and ultrasonography is becoming increasingly available, invasive studies, such as angiography, now seldom are performed.

Echocardiography

The chambers of the right side of the heart can be thoroughly interrogated by 2D ultrasonography and limited access also can be gained to the main pulmonary artery, a long segment of the right and a short portion of the left pulmonary artery in cats. Although heartworms are found most often in the main and right lobar branch of the pulmonary artery, it is necessary to probe methodically all of these locations since in a typical light infection, worms may occupy only one or two sites, and sometimes cannot be found at all. The body wall of an adult heartworm is strongly echogenic and produces short, segmented, parallel linear artifacts where the imaging plane transects the parasite’s convoluted body, producing these signature signs of live worms. Sometimes dead heartworms can be recognized by collapse of the parallel sides of the body wall. An adult heartworm is relatively long compared to the length of the pulmonary arteries in cats. Therefore, there is a better chance in cats than in dogs of finding heartworms extending from peripheral branches into proximal segments where they can be visualized. An experienced sonographer has a very good chance of making a definitive diagnosis in cats that are actually infected with adult heartworms, particularly when there are several worms. The high specificity of this examination can confirm heartworm infection of at least five months duration, in suspected cases.

Bronchoalveolar Lavage and Other Clinical Laboratory Testing

Tracheal wash cytology and differential white blood cell counts may reveal large numbers of eosinophils, four to seven months
postinfection. The absence of this provocative finding in tracheal washes and peripheral blood from more chronically infected cats does not preclude heartworm infection. Hematologic and blood chemical tests are nonspecific gauges of systemic illness and contribute nothing to confirm the diagnosis of FHD.

**Necropsy Confirmation**

Since making an antemortem diagnosis of heartworm infection may be difficult, necropsy confirmation should be attempted in cats suspected of dying of the disease or in which the cause of death is unexplained. A thorough search of the vena cavae, right side of the heart, and pulmonary arteries must be performed since one or two worms easily can be overlooked, particularly if immature, dead and fragmented, or in the distal extremities of the pulmonary arteries. Because heartworms occasionally are restricted to ectopic sites, the systemic arteries, body cavities and, if neurologic signs were present, the brain and spinal canal also should be examined thoroughly, when heartworms have not been found in the usual locations.

**TREATMENT**

**Medical Options**

Adulticide therapy, even in lightly infected cats, can be hazardous and should not be initiated simply on the basis of having diagnosed heartworm infection. If a cat displays no overt clinical signs despite radiographic evidence of pulmonary vascular/interstitial lung disease consistent with FHD, it may be prudent to allow time for a spontaneous cure to occur, rather than risk premature death by inducing postadulticide pulmonary thromboembolism. The course of infection in these subclinical cases can be monitored periodically at six to 12 month intervals by repeat antibody and antigen testing, and thoracic radiography. In those cats destined to recover, regression of radiographic signs and especially seroconversion to negative status provide evidence that the period of risk probably has passed.

Prednisone in diminishing doses often is effective medical support for infected cats with radiographic evidence of interstitial lung disease, whether or not they appear ill. Also, this should be initiated whenever antibody and/or antigen-positive cats display clinical signs. An empirical *per os* regimen is 2 mg/kg body weight/day, declining gradually to 0.5 mg/kg every other day by two weeks and then discontinued after an additional two weeks. At that time the effects of treatment should be reassessed based on the clinical response and/or thoracic radiography. This treatment may be repeated in cats with recurrent clinical signs.

Cats that become acutely ill need to be stabilized promptly with supportive therapy appropriate for treating shock. Depending on the circumstances, this may include intravenous adrenocorticosteroids, balanced electrolyte solutions, bronchodilators and oxygen via intranasal catheter or closed cage. Diuretics are inappropriate, even for infected cats with severe interstitial or patchy alveolar lung patterns. Aspirin and other nonsteroidal antiinflammatory drugs have failed to produce demonstrable benefit and actually may exacerbate the parenchymal pulmonary disease.

Adulticide administration is considered the treatment of last resort for cats in stable condition, but which continue to manifest clinical signs that are not controlled by empirical adrenocorticosteroid therapy. There are few occasions when this course of action would be elected. Consideration should be given to the following caveats:

1. Potentially fatal pulmonary thromboembolism must be accepted as a risk in attempting a cure. Even one heartworm represents a major source of emboli and
thromboembolic complications can be expected in approximately one-third of adulticide treated cats. Based on empirical experience with dogs, this risk increases for cats thought to be infected heavily, based on a strongly positive antigen test, and radiographic evidence of compatible pulmonary arterial and parenchymal disease.

2. Sodium thiacetarsamide administered at the dog dose of 2.2 mg/kg body weight twice daily for two consecutive days is an effective adulticide in cats. Although cats seem to be less likely than dogs to develop systemic toxicosis from this arsenical, they are at greater risk of pulmonary embolism and should be held in cage confinement under close observation for three to four weeks before they are considered out of danger. Adulticide treatment with thiacetarsamide will soon no longer be an option since production has ceased and the commercial supply has been liquidated.

3. There is insufficient experience with the adulticide, melarsomine dihydrochloride, in carefully monitored clinical trials to recommend its use in cats, at this time.

Surgical Options

In principle, it is preferable to remove heartworms rather than destroy them in situ. This can be accomplished successfully by either introducing brush strings or basket catheters via right jugular venotomy, or after left thoracotomy, alligator forceps can be inserted through a right ventricular purse string incision. Before attempting either approach, heartworms should be identified ultrasonographically in locations that can be reached with these inflexible instruments. When probing from the right jugular vein, worms must be present at the tricuspid valve or within the right atrium since access to the right ventricle cannot be achieved ordinarily with these instruments. Through a ventriculotomy incision, both atria and ventricle as well as the main pulmonary artery can be reached with straight alligator forceps.

Although it may not be possible to retrieve every worm, the surgical option may be a reasonable alternative to symptomatic support or adulticide treatment of cats that are heavily infected and display clinical signs. Surgery is specifically indicated in those few cases that develop the caval syndrome. Care must be taken to remove the worms intact since traumatic transection may cause acute circulatory collapse and death.

Surveillance of Infected Cats

Serologic retesting at six to 12 month intervals for the purpose of monitoring infection status is recommended for all infected cats, whether or not they have clinical signs that are treated empirically or are given medical/surgical adulticide therapy. Once adult heartworm infection has been diagnosed, monitoring will be most informative if both antibody and antigen testing are performed. The retesting interval should be consistent with the clinical circumstances. For asymptomatic cats, an annual retest may be adequate. Spontaneous or adulticide induced elimination of infection in antigen-positive cats ordinarily will be followed within four to five months by disappearance of detectable antigenemia. Once cats become antigen-negative and are clinically normal, further antibody retesting becomes optional since antibody may persist for an indefinite period after the parasites are gone. In those cats that were not previously antigen positive, declining antibody or complete seroconversion is indicative of a terminated infection. In those cats with pulmonary vascular and/or parenchymal lung disease, or in which heartworms have been identified echocardiographically, radiography and ultrasonography also may be very useful for monitoring the course of infection and disease.
CHEMOPROPHYLAXIS

Monthly chemoprophylaxis is a safe and effective option for cats living in areas where heartworm infection is considered endemic in dogs, and exposure to infective mosquitoes is possible. Many cats live more sheltered lives than do most dogs and are often confined indoors. Unless the home environment provides an effective barrier to the entrance of mosquitoes, these so-called indoor cats may also be at some risk. Cat owners should be advised objectively of the potential risk of heartworm infection in their community and for their cat’s living conditions, and allowed to make their own decision regarding chemoprophylaxis. When monthly heartworm chemoprophylaxis is elected, it should be administered within 30 days following the estimated seasonal onset of transmission and be continued within 30 days after that period has ended.

Drugs

Heartworm chemoprophylaxis can be achieved in cats with monthly doses of either ivermectin or milbemycin oxime per os, or topical selamectin. Although each is registered in the U.S. for this purpose, only ivermectin and selamectin are currently being marketed for use in cats. The individual monthly prophylactic dose of ivermectin is 24 µg/kg body weight in cats, four times the minimum recommended dose in dogs. The individual dose of milbemycin oxime for heartworm prophylaxis in cats is 2.0 mg/kg body weight, which is also four times the minimum recommended dose in dogs. However, the dose of selamectin (6-12 mg/kg) is the same in both cats and dogs. Administration of these drugs in cats is not precluded by antibody or antigen seropositivity. The efficacy of moxidectin, and diethylcarbamazine citrate for heartworm chemoprophylaxis in cats has not been evaluated.

Serologic Testing

Prospective heartworm antibody testing of asymptomatic cats is not generally advocated unless administration of chemoprophylaxis is being considered. Since seroepidemiologic data for most communities are presently meager, it behooves veterinarians to become familiar with the local risk potential by testing cats before initiating heartworm chemoprophylaxis. While guidelines are still being developed and evaluated, it is considered prudent to establish this serologic benchmark for future reference in the event it becomes necessary to retest a cat receiving chemoprophylaxis.

Although testing cats before starting chemoprophylaxis is recommended, there is less utility in doing so than is the case for dogs. This apparent contradiction reflects the differences in testing methods and test performance in the two hosts. Pretesting (screening) dogs is limited to documenting either heartworm antigenemia or circulating microfilariae, both of which are specific indicators of adult worm infection in a host that is significantly more likely to become infected. Many, if not most, cats that are antibody positive have only been transiently infected to the fourth larval stage. Distinguishing between sensitization to early nonpathogenic larvae and ongoing infection with adult heartworms based on antibody testing is problematic at this time and may require considerable additional clinical evaluation, incurring major expense. Although infection status may remain in doubt for an antibody-positive cat, it is still eligible for chemoprophylaxis. The fact that it has been exposed to at least fourth-stage larvae, confirms that this is indeed a cat at potential risk of developing FHD and reinforces justification for recommending chemoprophylaxis. Antigen testing healthy cats is not advocated since the yield of positive results in such a population is extremely low and cost ineffective. Since microfilaremia in cats is uncommon,
transient and below levels that might trigger an adverse reaction to microfilaricidal chemoprophylactic drugs, pretesting for microfilarias is unnecessary. Furthermore, antibody retesting of cats already committed to chemoprophylaxis provides no assurance of efficacy since sensitization from repetitive aborted precardiac larval infections is possible in cats that are repetitively exposed. Therefore, the primary reasons for heartworm testing cats are:

1. to establish an etiologic diagnosis in those individuals that, based on other clinical evidence, are suspected of being infected,
2. to monitor the clinical course of those that have already been diagnosed with FHD, and
3. to establish a baseline reference prior to initiating chemoprophylaxis.

These guidelines and explanations are based on current information. They can be expected to change in either substance or degree as additional experience with heartworm infection in the cat is gained.

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