Guidelines

2005 Guidelines for the diagnosis, prevention and management of heartworm (*Dirofilaria immitis*) infection in cats

Prepared and approved by the Executive Board of the American Heartworm Society

Officers: Charles Thomas Nelson President; John W. McCall, Vice President; Sheldon B. Rubin, Secretary-Treasurer, Lynn F. Buzhardt, Donald W. Doiron, Wallace Graham, and Susan L. Longhofer, Board Members; Jorge Guerrero, Symposium Chair; Carol Robertson-Plouch, Symposium Co-Chair; and Allan Paul, Editor

1. Preamble

These recommendations are based on the latest information presented at the 2004 triennial symposium of the American Heartworm Society. Revisions to the last recommendations, published in 2001, are based on new research and additional clinical experience.

2. Epidemiology

Heartworms are considered at least regionally endemic in each of the contiguous 48 states, Hawaii, Puerto Rico, U.S. Virgin Islands and Guam. Heartworm transmission has not been documented in Alaska and even with the importation of microfilaremic dogs, it is doubtful the climate this far north will permit maturation of infective larvae. Relocation of infected, microfilaremic dogs appears to be the most important factor contributing to further dissemination of the parasite. The ubiquitous presence of one or more species of vector competent mosquitoes makes transmission possible wherever a reservoir of infection and favorable climatic conditions co-exist.

A climate that provides adequate temperature and humidity to support a viable mosquito population, and also sustain sufficient heat to allow maturation of ingested microfilariae to the infective, third-stage larvae (L3) within the intermediate host is a pivotal prerequisite for heartworm transmission to occur. Intermittent diurnal declines in temperature below the developmental threshold of 57 °F (14 °C) for only a few hours retard maturation, even when the average daily temperature supports continued development. At 80 °F (27 °C), 10–14 days are required for development of microfilariae to the infective stage.
The heartworm transmission season in the temperate latitudes is greatly influenced by the amount of accumulated heat in the environment during the incubation of the larvae in the mosquito. The peak months for heartworm transmission in the Northern Hemisphere are July and August. Algorithmic predictions based on analysis of historical temperature records have consistently over-estimated actual transmission periods, confirmed independently by a variety of field studies, and appear to represent conservative guidelines. Under the most favorable conditions, these estimates range from less than 4 months in southern Canada to potentially all year in the subtropical zones of southern Florida and the Gulf Coast. The model predicts that heartworm transmission in the continental U.S. is limited to 6 months or less above the 37th parallel, i.e., the Virginia–North Carolina state line.

Where the prevalence is low, a nidus of heartworm infection may be detected which usually represents both a focal spread of infection and heightened awareness through increased testing. Once a reservoir of microfilaremic domestic and wild canids is established beyond the reach of veterinary care, eradication becomes improbable.

3. Biology of feline heartworm infection

There are significant differences between feline heartworm disease and its classical canine counterpart, and these are consistent with characteristics of partially adapted host–parasite relationships. Although cats are susceptible hosts, they are more resistant to infection with adult *Dirofilaria immitis* than are dogs. When dogs not previously exposed to heartworms are injected with 100 L3 larvae, approximately 75 adult worms develop in almost 100% of the dogs whereas in cats, 3–10 adult worms develop in 75% of the cats. These L3 larvae molt to L4 and L5 stages with some loss along the way but there is a very high mortality rate of the L5 as they reach the lungs 3–4 months after infection. 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 worms of the same sex. 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-*D. 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. Host preference by some of the most abundant vectors does favor the dog and may contribute to the lower prevalence of infection in cats. However, the *Culex* spp. mosquito, which is the most common species in many urban areas, feeds on both cats and dogs without preference. 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. Necropsy surveys of shelter cats have placed the prevalence of adult heartworm infections at 5–15% of the rate in unprotected dogs in a given area. Circulating microfilariae are seldom found in infected cats. When microfilaremias do develop in cats, they appear only about 1-week later (195 days postinfection at the earliest) than in dogs, but seldom persist beyond 228 days (7.5 months) postinfection. Since heartworms transplanted from cats are capable of resuming production of circulating microfilariae in dogs, it appears feline infections become occult due to host immune-mediated clearance of the microfilariae and perhaps a reversible suppression of microfilariae production.

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

4. Pathophysiology of feline heartworm disease

The clinical importance of heartworms is amplified in cats because even a small number of heartworms are potentially life-threatening. Although 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 worms in the pulmonary arteries 3–4 months postinfection. These early signs appear to be induced by an acute vascular and parenchymal inflammatory response. This initial phase is often mis-diagnosed as asthma or allergic bronchitis. This acute phase subsides as the worms mature. Evidence suggests that live heartworms are able to suppress immune function. This allows many cats to tolerate their infection without apparent ill effects until the mature worms begin to die, which initiates the second stage of disease. The degenerating parasites cause pulmonary inflammation and thromboembolism which results in often fatal acute lung injury which some believe to be similar to acute respiratory distress syndrome (ARDS). This reaction can occur as the result of even a single worm.

In dogs, the caval syndrome (dirofilarial hemoglobinuria) results partly from large numbers of heartworms relocating to the cavae and right atrioventricular junction, interfering with tricuspid valve function. Caval syndrome occurs rarely in cats because they usually are infected lightly. However, even one or two worms may cause tricuspid regurgitation and resultant 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 less common in cats than in dogs. Even when narrowing of a lumen is compounded by worm-induced thrombosis, bronchopulmonary collateral circulation usually is adequate to prevent infarction of the lung.

5. Physical diagnosis

5.1. Clinical signs and physical findings

Many cats tolerate their infection without clinical signs, or with signs manifested only transiently. Clinical signs associated with feline heartworm disease may be only a vague malaise or can comprise predominantly respiratory, gastrointestinal (e.g., emesis) or occasionally neurologic manifestations, chronically or acutely. 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 when worms reside in the right atrioventricular junction interfering with tricuspid valvular function. Anorexia and weight loss occur in some cats. Intermittent vomiting unrelated to eating is frequently reported and in endemic areas when no other cause is evident, should raise suspicion of heartworm infection. Other abnormalities, such as ascites, hydrothorax, chylothorax, pneuemothorax, ataxia, seizures and syncope have been reported but are uncommon. A peracute syndrome consisting of some combination of signs including respiratory distress, ataxia, collapse, seizures, hemoptysis, or sometimes sudden death may arise without warning.

6. 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. A willingness to pursue this high index of suspicion 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.

6.1. Microfilariae

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

6.2. Serology

Interpretation of antibody and antigen test results is complicated and a thorough understanding of the limitations of both tests is necessary in order to use these assays in a clinical setting with any confidence. The antigen test is the "gold standard" in diagnosing heartworms in dogs but because unisex infections consisting of only male worms or symptomatic immature infections are more common in cats, none of the presently available antigen tests can be relied upon to rule out heartworm disease in cats. The sensitivity of commercially available tests has increased and they are highly effective in detecting single adult female worm infections. In the cat, detectable antigenemia develops at about 5.5–8 months postinfection. Necropsy surveys of shelter cats have shown that 50–70% of infected cats have at least one female worm.

Antibody tests have the advantage of being able to detect exposure to both male and female worms as larvae of either sex can stimulate a detectable immune response as early as 2 months postinfection. Initial research reported the sensitivity of the feline antibody tests to be as high as 98% in experimentally infected cats with an equally high specificity. However, necropsy surveys of naturally infected cats from shelters have indicated a lower sensitivity ranging from 32 to 89%. A necropsy survey where eight different antibody tests were evaluated, 21 of 31 heartworm infected cats were negative on at least one antibody test. Each different antibody test has varying sensitivity to each stage of larval development, thus discordant results between test methods are common. These tests were performed on postmortem samples, which may have some affect on the sensitivity, but in another necropsy survey involving 10 heartworm positive cats, 50% were antibody negative on antemortem samples. A third report of 50 clinical cases from a university referral center had a 14% false antibody negative rate. These four studies reported a wide range in sensitivity and to understand the differences, the population tested and the timing of the test must be examined. In the first study on experimentally infected cats, 50–100 L3 were injected into heartworm naïve cats and the cats were followed for 6–9 months. This is a much larger challenge than occurs in nature and no data are available on whether the antibody level will decrease over the expected 2–3 year lifespan of an adult worm. The two necropsy studies represent cat populations more typical of those encountered in clinical practice. In the last study from a university referral center, 72% of the cats had clinical signs of disease. Limited evidence from these studies suggest that the antibody level in cats decreases with time as the parasite matures and that heartworm infected cats with clinical signs are more likely to be antibody positive than infected asymptomatic cats.

Correct interpretation of 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. Since both L5 larvae and adult worms are capable of causing clinical disease in the cat, both antibody and antigen test are useful tools and when used together increase the probability of making appropriate diagnostic decisions.

6.3. Thoracic radiography

Independent of serologic test results, radiography may provide strong evidence of feline heartworm
disease, 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 ventrodorsal 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 reliable marker, since
most cats do not develop pulmonary hypertension and
because the main pulmonary artery 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 uni-
que to feline heartworm disease. 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
feline heartworm disease, thoracic radiographs pro-
vide no evidence of infection.

Radiographic features suggestive of feline heart-
worm disease can be found in about half of the cats
suspected of being infected, based on historical and
physical signs. Also, about half of those cats with
pulmonary arterial enlargement indicative of feline
heartworm disease are antibody positive. Temporal
differences in the development of the parasite, host
immune responses and organic disease, as well as
spontaneous regression of lesions, may account for
discrepancies between radiographic, clinical and
serologic findings.

6.4. Echocardiography

The chambers of the right side of the feline heart
can be thoroughly interrogated by 2D ultrasonography
and limited access also can be gained to the main
pulmonary artery, and a long segment of the right and
a short portion of the left pulmonary arteries. 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 worms
in a typical light infection may occupy only one or two
sites and may escape detection. 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 body, producing
the 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 with 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 experi-
enced 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. In suspected cases, the high specificity
of this examination generally allows for confirmation
of heartworm infection of at least 5-months duration.
Quantification of worm burden is, nevertheless,
difficult because the potential serpentine positioning
allows echo beams to transect the worm in multiple
sites, giving multiple echo images and potentially
over-estimation of worm burden.

6.5. Necropsy confirmation

Since making an antemortem diagnosis of heart-
worm infection may be difficult, necropsy confirma-
tion 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.
7. **Treatment**

7.1. **Medical options**

If a cat displays no overt clinical signs despite radiographic evidence of pulmonary vascular/interstitial lung disease consistent with feline heartworm disease, it may be prudent to allow time for a spontaneous cure to occur. The course of infection in these subclinical cases can be monitored periodically at 6–12 month intervals by repeat antibody and antigen testing, and thoracic radiography. In those cats...
destined to recover, regression of radiographic signs and especially seroconversion of a positive antigen test 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 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 oral regimen is 2 mg/(kg body weight day), declining gradually to 0.5 mg/kg every other day by 2 weeks and then discontinued after an additional 2 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 corticosteroids, 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 non-steroidal anti-inflammatory 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 corticosteroid therapy. There is insufficient experience with melarsomine dihydrochloride at this time. Preliminary data suggests that melarsomine is toxic to cats at dosages >3.5 mg/kg. Ivermectin at 24 µg/kg monthly given for 2 years has been reported to reduce worm burdens by 65% as compared to untreated cats. Since most cats have small worm burdens, it is not worm mass alone that is problematic, but the “anaphylactic” type reaction that results when the worms die and an ARDS-like reaction occurs. This will likely also occur when the ivermectin-treated worms die but the extent of the reaction is unknown. To date, there are not any studies that indicate any form of medical adulticidal therapy increases the survival rate of cats harboring adult heartworms.

7.2. 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, basket catheters, or loop snares 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 within the cavae or right atrium since achieving access to the right ventricle is difficult 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/or are in critical condition. Surgery is specifically indicated in those few cases that develop the caval syndrome. Care must be taken to remove the worms intact since partial or complete traumatic transection of a worm may result in acute circulatory collapse and death.

8. Additional considerations for adulticide therapy

8.1. Wolbachia

Most filarial nematodes, including *D. immitis*, harbor obligate, intracellular, Gram-negative bacteria belonging to the genus *Wolbachia* (*Rickettsiales*). In infections with other filarial parasites, treatment with tetracyclines during the first month of infection was lethal to some *Wolbachia*-harboring filariae, but not to a filariae that did not harbor *Wolbachia*, and treatment of *Wolbachia*-harboring filariae suppressed microfilaremia. Similar prophylaxis studies with *D. immitis* have not been reported, but in one study, tetracycline treatment of heartworm-infected dogs resulted in infertility in the female worms. These bacteria also have been implicated in the pathogenesis of filarial
diseases, possibly through their endotoxins. Recent studies have shown that a major surface protein of *Wolbachia* (WSP) induces a specific IgG response in hosts infected by *D. immitis*. It is hypothesized that *Wolbachia* contribute to pulmonary and renal inflammation through its surface protein WSP, independently from its endotoxin component. Studies to determine the effects of suppressing *Wolbachia* populations with doxycycline prior to adulticide therapy will be required to determine the clinical utility of this therapeutic approach.

8.2. Surveillance of infected cats

Serologic retesting at 6–12-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 4–5 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 and because continued exposure, even with preventive therapy, will result in a positive test. 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.

9. 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 risk. In one retrospective study, approximately 25% of cats diagnosed with adult heartworms were considered indoor cats. Caregivers should be advised objectively of the potential risk of heartworm infection in their community and for their cat’s living conditions. When monthly heartworm chemoprophylaxis is elected, it should at least be administered within 30 days following the estimated seasonal onset of transmission and be continued within 30 days after that period has ended. Administering a preventive year-round also has merit due to the following reason: (1) activity against some common intestinal parasites and in the case of selamectin, external parasites, (2) increased compliance and (3) retroactive efficacy as a safeguard for inadvertent missed doses (for a more detailed explanation, consult the Canine Guidelines under the heading “Macrocyclic Lactones”).

9.1. Drugs

Heartworm chemoprophylaxis can be achieved in cats with monthly doses of either ivermectin or milbemycin oxime orally, or topical selamectin. Preventives should be started in kittens at 8 weeks of age and be administered to all cats in heartworm endemic areas during the heartworm transmission season. The individual monthly prophylactic dose of ivermectin is 24 μg/kg, milbemycin oxime 2.0 mg/kg and selamectin 6–12 mg/kg of body weight. 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.

9.2. Serologic testing

Since seroepidemiologic data for most communities is 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 4th larval stage. Distinguishing between sensitization to early migrating larvae and on-going infection with adult heartworms based solely on antibody testing is problematic and requires considerable additional clinical evaluation, incurring major expense. Although infection status may remain in doubt for an antibody positive cat, such cats are still eligible for chemoprophylaxis. The fact that it has been exposed to at least 4th stage larvae, confirms that this is indeed a cat at potential risk of developing feline heartworm disease and reinforces justification for recommending chemoprophylaxis. Using an antigen test to screen healthy cats is also an option taking into account their limitations (refer to chart in Diagnostic Testing section for limitations of both antibody and antigen test). The preferred method for screening would include both an antigen and an antibody test.

Since microfilaremia in cats is uncommon, transient and below concentration levels that might trigger an adverse reaction to microfilaricidal chemoprophylactic drugs, pretesting for microfilariae 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 feline heartworm disease;
3. and to establish a baseline reference prior to initiating chemoprophylaxis.

These guidelines are based on the latest information on heartworm disease. In keeping with the objective of the Society to encourage adoption of standardized procedures for the diagnosis, treatment and prevention of heartworm disease, they will continue to be updated as new knowledge becomes available.