

Highlights of the Current
Canine Guidelines for the

Prevention, Diagnosis, and Management of Heartworm (*Dirofilaria immitis*) Infection in Dogs



AMERICAN
HEARTWORM
SOCIETY
EST. 1974

Revised 2018

These recommendations, revised in 2018, supersede previous editions and are based on the latest information presented at the 2016 Triennial Symposium of the American Heartworm Society (AHS), new research, and additional clinical experience, and have been peer reviewed by independent experts.

The complete version of the 2018 Canine Guidelines can be found at the [American Heartworm Society's website](http://www.heartwormsociety.org).

Prepared by *Dr. C. Thomas Nelson, Dr. John W. McCall, Dr. Stephen Jones, and Dr. Andrew Moorhead*, and approved by the Executive Board of the American Heartworm Society (Officers: *Dr. Chris Rehm, President; Dr. Stephen Jones, Past President; Dr. Tony Rumschlag, Vice President; Dr. Bianca Zaffarano, Secretary-Treasurer; Dr. Patricia Payne, Editor; Dr. Doug Carithers, Symposium Program Chair; Board Members: Dr. Elizabeth Clyde, Dr. Brian DiGangi, Dr. Chris Duke, Dr. Andrew Moorhead, Dr. Charles Thomas Nelson, and Dr. Jennifer Rizzo;*

and Ex Officio Members: *Dr. Marisa Ames, Symposium Program Co-Chair; Dr. John W. McCall, Co-Editor; Dr. Chris Adolph and Dr. Edward Wakem.*

References by *Christopher Evans, MS, Research Professional II, Department of Infectious Diseases, College of Veterinary Medicine, University of Georgia.*

Thank you to our generous sponsors: Boehringer Ingelheim, Ceva, Elanco, Zoetis, Virbac, IDEXX, and Merck.



SUMMARY OF HIGHLIGHTS

- **Diagnostics:** AHS recommends annual antigen and microfilaria testing. (As the interpretation of diagnostics has become more complex, please see the “Microfilaria and Antigen Testing” section for more complete information.)
- **Prevention:** AHS recommends year-round administration of preventive drugs approved by the US Food and Drug Administration (FDA) to prevent heartworm infection and enhance compliance, the latter being particularly important in light of the documented presence of resistant subpopulations. Application of an Environmental Protection Agency (EPA) registered mosquito repellent/ectoparasiticide has been shown to increase the overall efficacy of a heartworm prevention program in laboratory studies involving known resistant heartworm isolates by providing control of the arthropod vector of heartworm. In addition, AHS recommends reduction of exposure to mosquitoes through standard environmental control of mosquitoes and their breeding environments, and when possible, reducing outdoor exposure during key mosquito feeding periods.
- **Adulticide Therapy:** AHS recommends use of doxycycline and a macrocyclic lactone prior to the three-dose regimen of melarsomine (one injection of 2.5 mg/kg body weight followed at least one month later by two injections of the same dose 24 hours apart) for treatment of heartworm disease in both symptomatic and asymptomatic dogs. Any method utilizing only macrocyclic lactones as a slow-kill adulticide is not recommended.

EPIDEMIOLOGY

- Heartworm infection has been diagnosed in all 50 states and around the globe.
- Environmental and climatic changes, both natural and those created by humans, relocation of microfilaremic dogs, and expansion of the territories of microfilaremic wild canids continue to be important factors contributing to further spread of the parasite.
- A pivotal prerequisite for heartworm transmission is a climate that provides adequate temperature and humidity to support a viable mosquito population, and can also sustain

sufficient heat to allow maturation of ingested microfilariae into infective, third-stage larvae within the intermediate host.

- The length of the heartworm transmission season in the temperate latitudes also depends on factors such as the influence of microclimates, unique biological habits and adaptations of the mosquito vector, variations in time of larval development, mosquito life expectancy, and temperature fluctuations.

Heartworm transmission does decrease in winter months, but the presence of microenvironments in urban areas suggests that the risk of heartworm transmission never reaches zero.

- The American Heartworm Society, in collaboration with the Association of Shelter Veterinarians, has developed a [protocol](#) to help minimize the risk of heartworm transmission associated with transportation and relocation of dogs.

For detailed information on heartworm epidemiology, please refer to the complete [AHS Current Canine Guidelines](#).

BIOLOGY AND LIFE CYCLE

- The relatively long [life cycle](#) of *D. immitis* (7 to 9 months) requires a reservoir of infection, a vector capable of transmitting infection, and a susceptible host.
- The mosquito, the required vector for transmission of *D. immitis*, becomes infected as she takes a blood meal from a microfilaremic host.
- The *D. immitis* microfilariae mature within the malpighian tubules of the mosquito, developing into larval stage 1 (L1), then molting into larval stage 2 (L2), and finally molting into the infective third-stage larvae (L3), which are transmitted to the dog when bitten by the mosquito.

- Once the infective L3 enter the dog's body, they molt into fourth-stage larvae (L4).
- A final molt into juvenile/immature adults occurs between days 50 and 70, while they are migrating through the body; and they eventually reach the smallest pulmonary arteries as early as day 67 after transmission.
- Sexual maturity occurs about day 120 post infection with dogs developing patent infections (i.e., having circulating microfilariae) as early as 6 months but usually by 7 to 9 months after infection.
- A clear understanding of heartworm transmission, development, prepatent period, and the susceptibility of the different life stages of the parasite to available pharmaceutical drugs is critical to the successful management of infected dogs.

For detailed information on heartworm biology and life cycle, please refer to the complete [AHS Current Canine Guidelines](#).

HEARTWORM PREVENTION

- The FDA-approved heartworm preventives currently marketed (ivermectin, milbemycin oxime, moxidectin, and selamectin) belong to the macrocyclic lactone (ML) class of drugs.
- Macrocyclic lactones, when given according to label instructions, are highly effective and are among the safest medications used in veterinary medicine.
- While the vast majority of reported claims of lack of efficacy of macrocyclic lactones can be linked to poor compliance, isolated pockets of resistant heartworm subpopulations have been documented, mainly in the southeastern US.
- Although an [algorithm](#) utilizing the microfilarial suppression test (MFST) to help clinicians evaluate cases of suspected resistance to macrocyclic lactones was recently developed, no definitive test for resistance exists, making determination of its distribution difficult.
- There is general agreement that resistance to experimental infections is concerning, and that the products now available are highly effective and should continue to be used as the manufacturers suggest.

- AHS and the FDA recommend year-round administration of FDA-approved preventive drugs to prevent heartworm infection and enhance compliance.

It is possible for an animal to become infected because of skipped or delayed administration of just one preventive dose, particularly in highly endemic areas.

- Application of an EPA-registered mosquito repellent/ectoparasiticide has been shown to increase the overall efficacy of a heartworm prevention program by controlling the mosquito vector in laboratory studies.
- In addition, reduction of exposure to mosquitoes through standard environmental control of mosquitoes and their breeding environments, and when possible, reducing outdoor exposure during key mosquito feeding periods is recommended.
- The risk management approach for heartworm disease in dogs is a process of qualitatively and quantitatively evaluating the threat of infection and disease followed by coordinated and reasonable application of countermeasures to mitigate each of those threats. The threat of heartworm infection can be readily assessed using the [AHS Incidence Maps](#).

For detailed information on heartworm prevention, please refer to the complete [AHS Current Canine Guidelines](#)

PRIMARY DIAGNOSTIC SCREENING

- The American Heartworm Society recommends annual screening for all dogs over 7 months of age with both an antigen and a microfilaria test.
- The current generation of heartworm antigen tests identifies most "occult" (adult worms present but no circulating microfilariae) infections consisting of at least one mature female worm and are nearly 100% specific.
 - Differences in sensitivity exist especially in

cases with low worm burdens and/or low antigenemia.

- Currently there are no verified tests capable of detecting infections consisting of only adult male worms.
- All positive antigen tests should be confirmed through additional testing prior to the administration of any therapy.
- Confirmation is accomplished upon the identification of circulating microfilariae, or when another positive result is obtained utilizing a different type of antigen test.

A negative antigen test result does not confirm that a dog is free of heartworm infection; it simply indicates that no antigen can be detected by that particular testing method.

- All dogs should be tested for microfilariae. Microfilaremia validates serologic results, identifies the patient as a reservoir of infection, and alerts the veterinarian to a high microfilariae burden.
- False-negative test results occur most commonly when infections are light, female worms are immature, only male worms are present, and/or the test kit instructions have not been followed. There are also suspected cases of antigen–antibody complexes interfering with antigen testing, resulting in false-negative tests.
- Heat treatment of serum samples prior to heartworm antigen tests to release blocked antigen is currently available through reference laboratories. However, the routine heating of blood samples IS NOT PRESENTLY RECOMMENDED for heartworm screening.
 - Rely on antigen and microfilaria testing for routine heartworm screening. These tests are highly sensitive and accurate.
 - Because heat treatment is contrary to labeling for in-house antigen tests and may interfere with the accuracy of certain blood tests, do

not heat-treat samples as part of routine screening.

- Consider heat treating a patient’s serum sample when a negative antigen test result does not correlate with the presence of circulating microfilariae, or when there is suspicion of active clinical disease.
- In cases of noncompliance or changing the brand or type of heartworm preventive, the dog should be antigen and microfilaria tested prior to starting or changing products.
 - A positive test indicates preexisting infection. The dog should always be retested 6 months later. A positive test at this time would most likely be due to an infection acquired before starting or resuming preventive therapy; however, in rare instances, an existing infection might be missed (i.e., false-negative test due mainly to young or low worm burden infection). Antigen and microfilaria testing should be performed on the one-year anniversary date of the initial test and annually thereafter.

DIAGNOSTICS FOR PRE-ADULTICIDE EVALUATION IN AN INFECTED DOG

- The extent of diagnostic testing necessary in the pre-adulticide evaluation varies depending on the clinical status of each patient. Selected clinical and laboratory tests should only be performed to complement information obtained from a thorough history, physical examination, and antigen and microfilaria tests.
- Key factors influencing the probability of post-adulticide thromboembolic complication and outcome of treatment are not easily measured with standard diagnostic procedures, including 1) the activity level of the dog, 2) the extent of concurrent pulmonary vascular disease, and 3) the severity of infection (high versus low worm burdens).
- Thoracic radiographs can assist in providing an assessment of the animal’s cardiopulmonary status and may be helpful in evaluating the potential for post-adulticide treatment complications.
- Restricting the dog’s activity is imperative as exercise, excitement, and overheating are harbingers of complications.

- Prior to treatment, the owner's ability and willingness to properly confine treated dogs should be thoroughly investigated. A helpful resource for pet owners, "[Battling Boredom: Tips for Surviving Cage Rest.](#)" is available on the AHS website.
- No set protocol has been established for pre-treatment workup and reasonable judgment should always be used to weigh the necessity, benefit, and extent of each diagnostic procedure performed.

For detailed information on heartworm diagnostics, please refer to the complete [AHS Current Canine Guidelines](#).

PRINCIPLES OF HEARTWORM TREATMENT

- The goals of any heartworm treatment are to improve the clinical condition of the animal and to eliminate all life stages of the heartworms (microfilariae, larval stages, juveniles, and adults) with minimal post-treatment complications.
- Dogs exhibiting significant clinical signs of heartworm disease should be stabilized before administering an adulticide; this may require administration of glucocorticosteroids, diuretics, vasodilators, positive inotropic agents, and fluid therapy.
- Melarsomine, administered via deep intramuscular injection into the belly of the epaxial lumbar muscles (between L3 and L5), is the only adulticidal drug approved by the FDA.
- Adjunct therapy with doxycycline for 4 weeks prior to the administration of melarsomine eliminates *Wolbachia*, an endosymbiont bacteria harbored within *D. immitis*, reduces pathology associated with dead heartworms, and disrupts heartworm transmission.
- A macrocyclic lactone preventive should be administered for 2 months prior to administering melarsomine to reduce new infections and eliminate existing susceptible larvae.
 - The effectiveness of the macrocyclic lactone can also be potentiated with concurrent use of doxycycline for 4 weeks, as this will essentially eliminate all developing larvae during the first 60 days of treatment.

Exercise restriction during the entire treatment and recovery period is ESSENTIAL for minimizing cardiopulmonary complications, as there is a distinct correlation between the activity level of the dog and the severity of disease.

- Caval syndrome, which develops acutely in some heavily infected dogs when adult heartworms partially obstruct blood flow through the tricuspid valve, usually ends fatally within 2 days if surgical extraction of the worms is not pursued promptly.
- Non-arsenical-based treatment protocols have been studied to guide management of dogs that are not candidates for melarsomine treatment. While non-arsenical treatment protocols have their place for a small percentage of dogs, it can take much longer to kill adult worms, during which time heartworm pathology and damage can progress.
- The treatment protocol recommended by the AHS (**Table 1**) includes pretreatment with an ML and doxycycline, following by a month-long waiting period, then 3 doses of melarsomine on days 60, 90 and 91. The AHS recommends this protocol for the following reasons:
 - Doxycycline in combination with ivermectin reduced *Wolbachia* numbers more effectively than doxycycline alone.
 - Waiting until day 60 to start killing the adult worms with melarsomine allows time for *Wolbachia* surface proteins and other metabolites to dissipate, as well as time for the heartworms themselves to wither.
 - This protocol has been shown to decrease respiratory complications and mortality associated with heartworm treatment.

For detailed information on heartworm treatment, please refer to the complete [AHS Current Canine Guidelines](#).

Table 1. AHS-Recommended Heartworm Management Protocol

Day	Treatment
Day 0	<p>In a dog diagnosed and verified as heartworm positive:</p> <ul style="list-style-type: none"> • Positive antigen (Ag) test verified with microfilaria (MF) test • If no MF are detected, confirm with second Ag test from a different manufacturer • Apply an EPA-registered canine topical product labeled to repel and kill mosquitoes • Begin exercise restriction—the more pronounced the signs, the stricter the exercise restriction <p>If the dog is symptomatic:</p> <ul style="list-style-type: none"> • Stabilize with appropriate therapy and nursing care • Prednisone prescribed at 0.5 mg/kg BID first week, 0.5 mg/kg SID second week, 0.5 mg/kg every other day (EOD) for the third and fourth weeks
Day 1	<ul style="list-style-type: none"> • Administer appropriate heartworm preventive <ul style="list-style-type: none"> ○ If MF are detected, pre-treat with antihistamine and glucocorticosteroids, if not already on prednisone, to reduce risk of anaphylaxis ○ Observe for at least 8 hours for signs of reaction
Days 1–28	<ul style="list-style-type: none"> • Administer doxycycline 10 mg/kg BID for 4 weeks <ul style="list-style-type: none"> ○ Reduces pathology associated with dead heartworms ○ Disrupts heartworm transmission
Day 30	<ul style="list-style-type: none"> • Administer appropriate heartworm preventive • Apply an EPA-registered canine topical product to repel and kill mosquitoes
Days 31-60	<p>A one-month wait period following doxycycline before administering melarsomine is currently recommended as it is hypothesized to allow time for the <i>Wolbachia</i> surface proteins and other metabolites to dissipate before killing the adult worms. It also allows more time for the worms to wither as they become unthrifty after the <i>Wolbachia</i> endosymbionts are eliminated.</p>
Day 61	<ul style="list-style-type: none"> • Administer appropriate heartworm preventive • Administer first melarsomine injection, 2.5 mg/kg intramuscularly (IM) • Prescribe prednisone 0.5 mg/kg BID first week, 0.5 mg/kg SID second week, 0.5 mg/kg EOD for the third and fourth weeks • Decrease activity level even further: cage restriction; on leash when using yard
Day 90	<ul style="list-style-type: none"> • Administer appropriate heartworm preventive • Administer second melarsomine injection, 2.5 mg/kg IM • Prescribe prednisone, 0.5 mg/kg BID first week, 0.5 mg/kg SID second week, 0.5 mg/kg EOD for the third and fourth weeks
Day 91	<ul style="list-style-type: none"> • Administer third melarsomine injection, 2.5 mg/kg IM • Continue exercise restriction for 6 to 8 weeks following last melarsomine injections
Day 120	<ul style="list-style-type: none"> • Test for presence of MF <ul style="list-style-type: none"> ○ If positive treat with a microfilaricide and retest in 4 weeks • Continue a year-round heartworm prevention program based on risk assessment described in prevention section
Day 365	<ul style="list-style-type: none"> • Antigen test 9 months after last melarsomine injection; screen for MF • If still Ag positive, re-treat with doxycycline followed by two doses of melarsomine 24 hours apart