



## BRINGING THE 17<sup>TH</sup> TRIENNIAL HEARTWORM SYMPOSIUM TO YOU

### Foreword

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AMERICAN  
HEARTWORM  
SOCIETY™  
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### OUR EXPERTS

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**S**ince the American Heartworm Society (AHS) was formed in 1974, heartworm researchers, veterinarians, students and others have convened every three years for a scientific conference featuring the world's leading experts on heartworm disease. Hosting this important symposium is one of the most important investments the AHS makes in fulfilling our mission of leading the veterinary profession and the pet-owning public in the understanding of heartworm disease.

The 2022 symposium, which took place September 8-11, featured 40 speakers from three continents and was attended by veterinary practitioners, researchers, and industry representatives from a dozen countries and 30 states. I personally came away with a renewed enthusiasm to do my part to combat heartworms in my practice, and to work with the AHS to continue building on public and professional outreach to both veterinarians and veterinary nurses.

While it is not possible to share all the information from the 2022 Triennial Symposium in just a few short pages, we wanted to reach you, our readers, with some of the key findings. In this Clinician's Brief supplement, we've posed a series of questions to a group of speakers and moderators who took the stage at the symposium. We hope the answers will be of value to you in your daily practice.



The Q&A that follows reflects the opinions of some of the leading experts on heartworm disease and is not intended as an official statement from the American Heartworm Society. For more information from the 2022 symposium, please visit our website at [heartwormsociety.org](http://heartwormsociety.org).

## RESEARCH ON NEW APPROACHES TO HEARTWORM PREVENTION

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**Q. Research is being conducted at the University of Pennsylvania to explore the potential to stop heartworm transmission at its source—the mosquito vector. Why is this approach being investigated?**



**Dr. Michael Povelones:**

New strategies to prevent heartworm infection in pets are needed. When we look at heartworm incidence maps from the past few years, it's clear that we're not seeing true reductions in incidence or transmission. Meanwhile, the presence of heartworm reservoirs, including pets that are not being properly cared for and species such as wild canids, limit what we can do to stop transmission. After studying approaches being developed by scientists who study other mosquito-borne diseases, including malaria and dengue fever, my laboratory became interested in developing technologies to block heartworms in the mosquito vector.

**Q. Your hypothesis is that it may be possible in the future to deworm mosquitoes. How would this be done?**

**Dr. Povelones:** In our research, we've seen that the mosquito's immune system is a critical component of its ability to transmit heartworms. Researchers who study dengue fever have associated mosquitoes with an insect-specific bacterium called *Wolbachia* that can stimulate the mosquitoes' immune response and make it less hospitable to the dengue virus. It both lowers disease transmission and propagates the bacteria within the local mosquitoes. So, rather than killing the mosquitoes, our goal with heartworms would be to replace them with



a population incapable of supporting the life cycle.

Building on that success, and with funding from the Morris Animal Foundation to explore this idea, we have generated preliminary data demonstrating that infected mosquitoes with non-genetically modified *Wolbachia* bacteria can prevent heartworm transmission by the mosquito and limit the development of drug-resistant parasites. It differs from strategies such as using insecticides to kill mosquitoes—an approach that invariably leads to resistance—or genetically modifying mosquitoes, which can be both controversial and difficult.

**Q. How might a better understanding of how heartworms interact with their animal hosts improve or speed the development of new types of heartworm preventives?**



**Dr. Timothy Geary:** In order to evolve and survive, animals must learn to utilize their immune systems to resist almost all parasites. Heartworm is a great example of what we call "host-parasite specificity" because heartworms develop by reproducing in permissive hosts. Dogs, coyotes, canids and, to some extent, cats are all permissive hosts for heartworm. The goal of my research is to figure out how to transform a permissive host into a non-permissive one.

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—Dr. Timothy Geary

This requires understanding how heartworms exchange chemical information with their hosts—what I call a “molecular dialogue.” If we can understand that dialogue, I think we will be able to change dogs into non-permissive hosts for *Dirofilaria immitis*.

**Q. How have lab animal models helped advance other types of disease management research—and how might such an approach advance the science of heartworm management?**

**Dr. Geary:** With heartworms, it is extremely difficult and expensive to conduct experiments in dogs because the heartworm life cycle lasts so long. It also presents ethical challenges because no one likes to conduct terminal research on dogs. Lab animal models have been essential in advancing biomedical research. By using our findings about the genome of one species and translating those findings into lab animal models, such as mice or rats, we can conduct research that is more humane and economical.

Macrocytic lactones like ivermectin, moxidectin, milbemycin and others that are

used for heartworm control today have been a mainstay of veterinary practice in much of the U.S. for decades now. They’ve truly been a miracle class of drugs. However, that control is threatened by the development of heartworms that are resistant to this class of medications, and we need new molecules that can supplement, complement, or even replace them. It’s a very tall order, but we have examples from approaches developed to control human parasitic disease that may flow back into veterinary medicine and provide a potential solution to some of our resistance problems. I’m very optimistic that we will find new ways to solve this problem.

**NEW DEVELOPMENTS IN HEARTWORM DIAGNOSIS AND PATIENT EVALUATION**

**Q. What potential is there to develop easier—and earlier—ways to detect heartworms in dogs?**



**Dr. Lindsay Starkey:** There has been a lot of work done recently to enhance our ability to diagnose heartworms and to find diagnostic strategies

that might be better for pets and/or easier for clients. For example, researchers at Texas A&M have looked at microRNAs that are secreted by heartworms and detectable in the blood and different body fluids—and potentially able to reliably serve as markers for earlier heartworm diagnosis before the animal is six to seven months post-infection.

This work is significant, because we know that damage from heartworm infection begins to take place well before a dog can even test positive on an antigen test. With earlier diagnosis, we can ensure the dog is started on both a heartworm preventive and doxycycline, along with exercise restriction, and be ready





for melarsomine treatment as soon as the heartworms are old enough to be susceptible. Meanwhile, with novel treatments that may be available in the future, we might be able to initiate treatment earlier yet. Finally, researchers

**“If a veterinarian suspects a negative heartworm test result is a false negative and subsequently gets a positive result following heat treatment of the blood sample, he or she can feel confident with that result.”**

**– Dr. Lindsay Starkey**

are looking at the potential to detect heartworm antigen in the urine and the breath as less-invasive alternatives to antigen detection in blood.

**Q. The potential for getting a false-negative result is one of the challenges that can confound heartworm diagnosis in pets. What have we learned lately about factors involved in immune complex formation and dissociation of heartworm antigen in blood samples?**

**Dr. Starkey:** One concern of veterinarians with heartworm diagnosis is the prospect of missing a diagnosis despite having conducted a heartworm test. Fortunately, both heat and

acid treatment can help dissociate immune complexes that can be a cause of false-negative results.

Nevertheless, the fear has persisted that such techniques might lead to false-positive results on heartworm tests. Nobody wants that to happen, because you don't want to treat a dog with melarsomine if it doesn't need it! The good news is that recent data suggest that neither heat nor acid treatment produces false-positive results, even in animals infected with other parasites. If a veterinarian suspects a negative heartworm test result is a false negative and subsequently gets a positive result following heat treatment of the blood sample, he or she can feel more confident in that result.

## **HEARTWORM DISEASE IN CATS**

**Q. What have recent studies told us about the incidence of heartworm—and relative risk—in cats?**



**Dr. Jessica Rodriguez:**

Knowing that only a relatively small percentage of cats leave veterinary offices with heartworm disease preventives, we decided to study the risk of heartworm infections in cats compared to dogs in a geography we already knew to be endemic for canine heartworm. A drawback with some previous incidence studies is that they usually looked only at the results of heartworm antigen tests, which can only detect the presence of adult worms. We included heartworm antibody testing as well, because a positive antibody test tells us a cat has been bitten by an infected mosquito and that, at a minimum, the L3 larvae have molted to the L4 stage.

We partnered with the University of Florida (UF) and Oklahoma State University to conduct our study, which was approved by the UF

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Institutional Animal Care and Use Committee. We collected blood samples from 100 dogs and 100 cats in central and south Florida that were age- and geography-matched and had no history of being on heartworm preventives. We ran an array of heartworm tests on these animals—antigen testing, antigen testing with heat-treated serum samples to dissociate immune complexes (which can increase the sensitivity of antigen tests), microfilaria testing, and antibody testing in cats. We considered a dog or cat to be heartworm-positive if they were positive on at least one of those tests.



### Q. What were the results?

**Dr. Rodriguez:** Looking at antigen testing alone, dogs had significantly higher heartworm prevalence. This was not surprising since dogs are more likely to become infected with patent adult heartworm infections than cats. We also didn't see any heartworm microfilariae in the cats which, again, was expected. However, when we looked at antibody testing, we found several positive cats. In fact, when we compared the prevalence of heartworm in dogs vs. cats, we found no statistical difference in prevalence between the two species.

### Q. Why is managing heartworm disease in cats so challenging?



**Dr. Tom Nelson:** There are multiple reasons why veterinarians don't understand and don't diagnose feline

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**—Dr. Jessica Rodriguez**

heartworm disease. The leading reason is that most of them have never seen it. There's an old saying: “You won't find what you don't look for and you don't look for what you don't understand.” While adult heartworms in dogs cause cardiovascular disease, in cats, heartworm disease is primarily a pulmonary and airway disease caused by the presence of immature larvae in the vasculature.

A further complication of feline heartworm diagnosis is that if practitioners suspect feline heartworm infection, they typically send a blood sample out for an antigen test. This is a very good test for detecting heartworms in dogs, but it is not ideal for most feline infections, because most heartworm disease in cats is not caused by adult heartworms.

### Q. How should veterinarians approach diagnosis in cats?

**Dr. Nelson:** In my opinion, any cat that presents to a practice with cough in a heartworm-endemic area should be tested for heartworms, because it is a big issue. A practitioner can do an antigen test, but I recommend that the blood sample be heat treated prior to running the test to increase the sensitivity. I would also send the

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sample off for an antibody test. While antibody tests admittedly have some drawbacks, the results can at least provide you with more information about the cat's exposure history. If the antigen test is negative and the antibody test is positive, you will know that the cat had immature worms and probably has vascular disease.

In cases where feline heartworm disease is suspected, I also recommend doing radiographs and looking for changes in the caudal lobar arteries—typically in the left one where the artery crosses the 9th rib. If the artery is 1.6 times the width of the rib, it is a classic sign of immature heartworms in the cat.



### **Q. What about treatment of cats with adult worms? With no approved treatments, what can practitioners do?**

**Dr. Nelson:** With no treatment, 20 percent of cats with adult worms will die within three to four years. While we don't have the option of using melarsomine, there are some things a veterinarian can do.

If the cat is showing clinical signs, we can use a reducing dose of prednisolone. We can also administer a course of doxycycline, just as we do in the dog. I recommend starting at a lower dose, using 5 mg/kg twice a day and use the suspension vs. pills to avoid the risk of esophagitis. The cat should also be on prevention as well. By treating with doxycycline and preventive, we can limit the

*Wolbachia* and the worms will eventually die. I also recommend putting the cat on an anti-leukotriene such as montelukast, because we know heartworms produce interleukin-4 and interleukin-8 cytokines.

## **EVALUATION OF HEARTWORM-POSITIVE DOGS**

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### **Q. Which imaging tests should be used when evaluating dogs with heartworm infection?**



**Dr. Marisa Ames:** The three most common imaging modalities are thoracic radiographs, point-of-care ultrasound and echocardiography.

Thoracic radiographs are the most widely available and the most performed diagnostic imaging test. However, they are not always necessary. An otherwise healthy dog that has no clinical signs—or only minimal signs, such as an intermittent cough—will probably tolerate adulticide therapy well and not require extensive evaluation. Taking radiographs in an asymptomatic dog to serve as a baseline is never wrong, but if cost is a concern, I would prioritize treating the dog. A persistent cough is probably the most common indication for thoracic radiographs in dogs with heartworm infection. A common finding is pneumonitis caused by inflammation from the worms themselves or from the death of microfilariae. Radiographic signs of pneumonitis include a bronchial or bronchointerstitial pattern.

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**—Dr. Marisa Ames**





## WHAT'S NEW IN HEARTWORM TREATMENT?

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**Q. Heartworm treatment protocols, and the potential for alternative protocols and medication dosing was discussed at the symposium. What were some of the key takeaways?**



**Dr. Andy Moorhead:** One area of debate pertains to the administration of doxycycline in eliminating the *Wolbachia* bacteria that play a role

in the development of heartworms in the host animal. It's been shown that if you administer doxycycline for four weeks to a heartworm-positive dog, you will find that some microfilariae survive; meanwhile, if you take those microfilariae and feed them to a mosquito, there will still be development of a third-stage infectious larvae. However, if you take those larvae and put them into another dog, there will be no development of adult heartworms. One of the big questions we have is, exactly where does this stopgap occur? Are we preventing molting or are we interfering with the interaction between *Wolbachia* and the animal's immune system?

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**—Dr. Andy Moorhead**

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If the dog has more advanced clinical signs, such as lethargy, shortness of breath or syncope—which suggests pulmonary hypertension or right-sided heart dysfunction—radiographs will allow you to evaluate for pulmonary dilation and/or changes to the shape of the right heart. If a practitioner suspects the presence of fluid, point of care ultrasound can be a useful means of quantifying the amount of fluid and removing it if warranted. Removing pleural fluid also ensures higher quality thoracic radiographs. Practitioners with more experience can also use ultrasound to image the heart and look for intracardiac worms in the right ventricle and atrium.

In heartworm-positive dogs without clinical signs, echocardiography is usually not indicated. Echocardiography is most useful when the radiograph is clearly abnormal, and the dog has clinical signs (frequent cough, shortness of breath, lethargy, or collapse). Questions that can be answered would include: (1) Does the dog have pulmonary hypertension and, if so, what severity? (2) Does the dog have right-sided heart dysfunction and, if so, how severe? (3) If a murmur is present, is there disruption of the tricuspid valve by worms or remodeling of the right heart? In these cases, echocardiography can help determine whether therapies such as sildenafil or pimobendan are needed.

need to wait to give melarsomine. We hope to have answers to some of those questions soon.

Finally, there has been evidence from countries such as Brazil, where doxycycline is routinely administered to treat tick-borne disease, that resistance to doxycycline could be developing. We don't have a definitive solution for this yet, but we did hear presentations about testing that is underway on a new anti-*Wolbachia* medication for human patients. If proven to be safe and effective, such a medication could hold promise for veterinary patients as well.

**Q. Shelter practitioners face numerous challenges in balancing their limited resources with the need to treat—as well as diagnose and prevent—heartworms in pets. How can practitioners successfully perform this balancing act?**



**Dr. Brian DiGangi:** Surveys conducted by the Association of Shelter Veterinarians (ASV) have told us they need structured guidance for clinical decisions

that fall outside the normal guidelines or that don't follow a textbook scenario—for example, an animal that initiates treatment in a shelter but completes it in its new veterinarian's office.

The ASV and the AHS developed an algorithm [www.shelterhwtool.com] to help both shelter and private-practice veterinarians make evidence-based decisions that could fill in some of the gaps left by standard published recommendations. The algorithm answers a variety of questions, such as "Will we admit and treat dogs with heartworm disease to our shelter?", "Where will dogs be housed during heartworm treatment?", and "How will we



make sure treated dogs are staying behaviorally healthy during the period of rest and recovery during treatment?"

One of the keys to successful management of a complex disease like heartworm disease, whether it is in a shelter practice or a private practice setting, is to recognize that there are many definitions of success. As our profession faces increasing demands on our time and expertise, it is important to recognize that there may be a spectrum of options to approach disease management. By embracing this outlook, we can make sure that treatment is practical and affordable and meets the needs of the client and patient.

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