



BRINGING THE 14TH TRIENNIAL HEARTWORM SYMPOSIUM TO YOU

Foreword

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**AMERICAN
HEARTWORM
SOCIETY™**
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The American Heartworm Society (AHS) was created in 1974 as a not-for-profit organization dedicated to leading the veterinary profession and the pet-owning public in the understanding of heartworm disease. Our organization's goals are to further scientific progress in the study of heartworm disease, while encouraging and promoting effective procedures for its **diagnosis, treatment** and **prevention**.

One of the functions in the AHS charter is to convene a membership meeting and scientific symposium every three years on the latest information and research on heartworm disease. Our 2013 symposium, held September 8–10, in New Orleans, was one of the most important symposia held since the AHS was formed 40 years ago. In recent years, significant work has been done to better understand the issues faced by practitioners today, from the development of heartworm resistance to common preventives, to the complexities of feline heartworm, to the role *Wolbachia* plays in the pathogenesis of the disease. Information on these topics, as well their connection to the challenges of compliance, owner education and shelter medicine, sparked lively discussion in New Orleans.

The 2013 Triennial Heartworm Symposium included more than 50 presentations and posters. While it's not possible to share three days of presentations and panel discussions from the Triennial Symposium in just a few short pages, we wanted to bring you some of the highlights. In this supplement, we posed questions to a group of speakers who took the stage at the symposium and captured their conclusions about some of the important topics discussed. We hope the answers will prove interesting and of value to you in your daily practice.

OUR EXPERTS

Clarke Atkins, DVM, DACVIM

Professor Emeritus, Medicine and Cardiology
North Carolina State University

Ray Kaplan, DVM, PhD

Professor, Department of Infectious Diseases
University of Georgia

Laura H. Kramer, DVM, PhD, Dipl. EVPC

Associate Professor of Veterinary Parasitology
University of Palma Veterinary School

Byron Blagburn, PhD

Distinguished University Professor
Auburn University

Ray Dillon, DVM, DACVIM

Professor, Dept. of Clinical Sciences
Auburn University

Katherine Polak, DVM, MPH

Maddie's Shelter Medicine Program
University of Florida

LACK OF EFFICACY AND HEARTWORM RESISTANCE

Q. What do we know about heartworm resistance at this point in time?



DR. KAPLAN: Over the past 10 to 15 years, there have been increasing reports of lack of efficacy (LOE), raising the possibility that macrocyclic lactone (ML) resistance in *D. immitis* is evolving. Though it is clear that the large majority of LOE cases are due to owner compliance failures, there is now compelling evidence that resistance to ML in *D. immitis* is real. So the questions then arise: why has resistance developed, and why does it seem to be concentrated almost exclusively in the Mississippi Delta region?

“ Though it is clear that the large majority of LOE cases are due to owner compliance failures, there is now compelling evidence that resistance to ML in *D. immitis* is real. ”

—Dr. Ray Kaplan

Based on our current understanding of the factors most important in driving the development of anthelmintic resistance in gastrointestinal nematodes (GIN) of livestock, areas where refugia are highest should be slowest to develop resistance. Yet the current patterns are in direct conflict with this assumption; resistance has developed in the precise area where refugia are highest. Likewise, after resistance in GIN reaches recognizable levels in a region, it rapidly spreads to other farms and other regions. In fact, various surveys of resistance prevalence performed in livestock across geographic regions demonstrate variability only in magnitude; the patterns are always quite similar. Again, the pattern in heartworms stands in stark contrast to this.

It has been 10 to 15 years since LOE reports began to increase greatly in the Delta and eight years since Hurricanes Katrina and Rita, when thousands of heartworm-infected rescue dogs from Louisiana and Mississippi were relocated throughout the United States. Despite this long passage of time, which should have provided great opportunities for amplification and spread of resistance, cases still

seem to be centered in the Delta; thus, there appear to be epidemiological circumstances that are particular to the Delta region with regard to driving the development and spread of drug resistance in heartworm. The Mississippi Delta has both high levels of infection in dogs and extremely large mosquito populations, which together produce levels of heartworm transmission much greater than in other areas of the USA. It is likely that these epidemiological circumstances provide the combination of genetic and biological factors necessary for drug resistance to evolve in heartworms.

Some parasitologists have implicated the practice of soft-kill or slow-kill therapy as playing a major role in the development of heartworm resistance; however, at present there is no scientific evidence that slow kill is a major risk factor for causing resistance. Rather, once resistant worms are established in a given area, it is possible that this practice could increase the rate of further development and spread. More research is needed before we can determine the true risk factors for the development of resistance in heartworm.

DR. ATKINS: The significance of slow-kill methodology in the development of resistance is an area of considerable debate. Some believe that slow kill is the cause of all resistance; others think that it may well have contributed but is one of many factors.

“ In my opinion, the most important item on the agenda right now is a diagnostic test for resistance. ”

—Dr. Byron Blagburn

Q. What kind of information on heartworm resistance is needed? What research will move us forward?



DR. BLAGBURN: The question that troubles veterinarians most is whether or not resistance is important in *their* area to *their* patients. With travel and pet movement, heartworm-positive dogs can be moved from one region to another and introduce resistant heartworms in new areas. In my opinion, the most important item on the agenda right now is a diagnostic test for resistance.

With the right genetic test, we'll be able to come into a veterinarian's practice area and sample area dogs—perhaps shelter dogs—and come back and tell them what percentage of dogs sampled in their area appear to carry the resistant genetics. I think within a short time we will be able to do that.

Q. Are you concerned that the current information about resistant heartworms will steer the focus away from compliance?



DR. ATKINS: I would stress to everyone that this is not a warning against using macrocyclic lactones—it's a caution to use them *correctly*. I'd also point out that lack of efficacy is a multifactorial problem, and the existence of resistant strains is just one factor.

“ Compliance is something we can affect *today*. ”

—Dr. Clarke Atkins

Compliance should always be a concern. In fact, the data I've helped gather would suggest that compliance plays a role in well over 95 percent of cases of heartworm infection. If we do see fewer cases of lack of efficacy, I think it will be due to better communication and education about heartworm prevention. That includes taking steps such as housing dogs indoors at night and/or in screened enclosures to minimize exposure to mosquitoes. The good news is that compliance is something we can affect *today*.

Q. What should practitioners do in the meantime?

DR. BLAGBURN: We do know that in a few instances, in certain parts of the country, there are heartworms that are resistant to preventives. But what we shouldn't presume is that the preventives aren't working. Most are working most of the time—and working very well. So the important thing for the veterinarian to remember is to continue to use the products as directed, at recommended intervals year-round and to continue to test as many dogs annually as they can.

REVIEW OF WOLBACHIA AND DOXYCYCLINE

Q. What is the significance of treating *Wolbachia* in cases of heartworm disease in dogs? And what's new?



DR. KRAMER: *Wolbachia* is known as an endosymbiont with heartworm, meaning that it is harbored within the worm's tissues, in particular in the female reproductive system. The role of *Wolbachia* is significant in the pathogenesis of heartworm disease for several reasons:

- It is essential for the long-term survival and reproduction of heartworm.
- It contributes to the complications of adulticide treatment. When adult heartworms die—whether spontaneously or because of treatment—they release large amounts of these bacteria. This, along with dead worm detritus, likely plays a role in the severity of post-treatment thromboembolism and pulmonary inflammation.

“ It's really a 'one-hand-washing-the-other' kind of relationship between the worm and the bacteria. ”

—Dr. Laura Kramer

I think the role of *Wolbachia* bacteria in the pathogenesis of heartworm disease is one of the most important discoveries made in recent years. During the symposium, we shared new information about a genomics study that is helping us understand the nature of the interdependency between heartworm and *Wolbachia*. It's really a “one-hand-washing-the-other” kind of relationship between the worm and the bacteria. The most recent research has shown that if we eliminate *Wolbachia* from heartworm-infected dogs through antibiotic treatment with doxycycline, not only do we reduce the detrimental, pro-inflammatory effects that follow worm death, but we also help block transmission of the parasites by greatly reducing circulating microfilariae.

When heartworm-positive dogs are treated with doxycycline, there are profound changes in the worms they carry.

The uterine content of female worms is significantly reduced—in fact, the uterus of the worm practically disappears. As a result, microfilarial counts go down very quickly, and the few microfilariae still circulating will likely not be transmitted to the mosquito vector. This enables us to block transmission of heartworms and, possibly, the development of resistant heartworm strains.

Q. How does doxycycline fit into a heartworm treatment protocol?

DR. KRAMER: Doxycycline is a bacteriostatic antibiotic that stops *Wolbachia* from replicating. The inflammation in the lungs that we see after worms die is much lower than if we hadn't used the antibiotic before we killed the worm.

The AHS guidelines call for pretreating the dog with doxycycline and macrocyclic lactones before using melarsomine to reduce the postadulthood side effects.

Another potential use is to combine the two as an alternative adulticide. Used in this manner, the adulticide effects are actually very potent—about 80 percent—after six to 10 months of therapy.

Q. But isn't that slow kill?



DR. KRAMER: As a researcher who has studied the combination of macrocyclic lactones with doxycycline—in my case, I did my work with ivermectin, but Dr. John McCall has done similar studies with moxidectin—I would classify slow kill as using a preventive alone to treat heartworm. When you use the two drugs together, you're doing something different to kill that worm. The worm dies faster with fewer side effects, because dogs usually are not symptomatic. Obviously this approach requires further discussion.

HEARTWORM DIAGNOSTICS

Q. What are the options for heartworm testing in dogs, and what are the pros and cons to the different options?

DR. BLAGBURN: There are differences in the tests that you conduct in-house and those you send to a reference laboratory. Some are more sensitive, are easier to perform,

take more or less time to perform, and are more or less costly than others. Some are easier to read than others. I happen to prefer in-clinic testing. I think veterinarians and staff members know much more about heartworm in their patients and in their practice areas than others do. In my opinion, given the ease of use, cost and availability, I would prefer to see the veterinarian do it.

Q. The results of antigen and microfilaria tests sometimes conflict. Can you explain why antigen-negative dogs sometimes have microfilariae?



DR. BLAGBURN: With a negative antigen test on a dog, the veterinarian assumes there are no adult worms in the bloodstream. That same dog, however, can be positive for microfilariae. There are a number of reasons this can occur, but several include:

- There could be adult worms there, but the antigen test isn't sensitive enough to detect them.
- The adult worms were there at one time, but have died and are past the point of detection.
- A prior veterinarian treated the dog for heartworm and eliminated the adult worms, but failed to eliminate microfilariae. This immature stage can persist in the dog's bloodstream for many months.
- Veterinarians should also remember that in rare instances, microfilariae can be passed from dam to pup during gestation. These pups are, of course, too young to have adult heartworms.

So, there are complications. What I tell my students is that there are four factors you have to understand:

- **Heartworm biology.** Where is the heartworm in the dog and what stage is it?
- **Preventive spectrum.** What does and doesn't the product eliminate? Different products may be effective against different stages of developing parasites.
- **The adulticide.** Efficacy depends on the sex and age of worms present. The adulticide efficacy can vary in individual dogs, depending on the worm burden. It will also depend on the regimen that the veterinarian uses.

- **Diagnostic tests.** What are their limitations? Some are more sensitive and specific than others, and some may detect earlier or later states than others.

These four factors can interact with each other in complicated ways. One of my favorite statements is “heartworms will find a way to fool you.” That’s because of all the variables involved.

Q. What should a veterinarian do when a patient’s heartworm status isn’t clear-cut?

DR. BLAGBURN: I favor a conservative approach. When a patient’s heartworm tests are conflicting or unclear, my best advice is to practice watchful waiting. In the meantime, keep the patient on prevention because we want to protect the dog from further infection. You can always test later on and see if an infection is maturing or if another test might detect it.

“ Heartworms will find a way to fool you... because of all the variables involved. ”

—Dr. Byron Blagburn

HEARTWORM AND OTHER PARASITIC LUNG DISEASES IN CATS

Q. How common is feline lung disease?



DR. DILLON: The incidence of feline lung disease is more common than many people realize because much of it is subclinical. The disease affects a cat’s quality of life without necessarily causing overt clinical signs of coughing or dyspnea. But if you look at lung disease based on radiographic surveys or histopathology of clinically normal cats, it’s very, very common. Over half of all shelter cats have some significant lung disease, and more than half exhibit radiographic abnormalities that most veterinarians would call bronchial disease.

Q. What can you tell us about your research on feline heartworm disease?

DR. DILLON: My focus is on the heartworm-associated respiratory disease (HARD) story. We’re able to show that infective heartworms molt from L3 to L4 to L5, and then reach the lung where most will die, creating serious lung disease as soon as three months after infection, even though adult worms may never develop. Frequently one finds neither the antigen in the blood nor evidence of adult worms. What you will find is severe inflammatory lung disease and peribronchial inflammation. It’s a very common presentation. If you think of feline heartworm disease in those terms, rather than, as in the dog, detecting adults in the right ventricle and pulmonary artery, feline heartworm disease is at the same incidence as canine heartworm disease for a given region.

“ While the clinical importance of HARD is still unclear, it appears to be present in over half of the cats infected with heartworms. ”

—Dr. Clarke Atkins

Q. How does heartworm infection present in cats, and how is it different from heartworm disease in dogs?



DR. ATKINS: Heartworm infection in cats is an important disease in heartworm-endemic areas. It is particularly devastating in cats because there is no practical therapy if a heartworm-infected cat progresses to a mature adult infection.

The clinical presentation of heartworm infection in cats is variable. When a mature infection occurs, the disease is not unlike its canine counterpart, even though the number of adult worms is much lower in the cat. The development of HARD, which occurs in infected cats even when the infection is aborted prior to maturation of the infection, is a situation unique to the cat. The pathology is evident in the pulmonary vessels (hypertrophy and inflammation), the airways (inflammation), and the lung parenchyma (eosinophilic pneumonitis). While the clinical importance of this syndrome is still unclear, it appears to be present in over half of cats infected with heartworms. That level of disease prevalence makes a strong argument for routine administration of heartworm preventive to cats.

Q. What new information do we have about differential diagnosis of heartworm in cats?



DR. DILLON: In my work over the years, it became obvious to me that we were missing differentials in our diagnosis of feline lung disease. I couldn't explain how all the cases we were seeing could be related to heartworm disease *alone*. So we looked further into the other parasitic diseases. The most obvious one was roundworms (*Toxocara cati*). We demonstrated that the associated lung lesion is almost indistinguishable from the classic lesions of heartworm seen on radiographs. In addition, lung lesions associated with *Aelurostrongylus* infection can also look very similar.

What disturbs me about the roundworm infections in cats' lungs is that the preventive medications apparently do not alter lung migration. They protect the cat against the adult GI parasite, but seem to attenuate, but not prevent, the lung damage. Heartworm disease is a cleaner story. Our research tells us that if you start heartworm prevention in cats before the heartworm has a chance to infect the cats—in other words before the mosquito season—you are able to prevent HARD, and even the antibody response that often confuses diagnostics. Roundworm and heartworm lung diseases are similar, but the practitioner should be aware that our hands are tied when it comes to preventing roundworm-induced lung disease with current preventives.

“ What disturbs me about the roundworm infections in cats' lungs is that the preventive medications apparently do not alter lung migration. ”

—Dr. Ray Dillon

Q. What should people do with this information?

DR. DILLON: They should just be aware that we have significant limitations. We don't have a magic way to differentiate these diseases. In fact, they are restrictive lung diseases, where the inability to take in good tidal volumes greatly inhibits a cat's exercise tolerance over time. And because cats are sedentary animals, the

disease can progress for a long time before the client actually notices significant change. And then it's too late.

I think we have to go back and realize that we've been wrong in a lot of our assumptions about feline lung disease and the differential list. If we're going to figure this out, we have to be more aggressive about diagnosing earlier and developing tests that diagnose these diseases more accurately.

MANAGING HEARTWORM IN THE SHELTER ENVIRONMENT

Q. What are the unique challenges faced by shelters in dealing with heartworm disease?



DR. POLAK: Shelters deal with an extremely large volume of animals—an estimated 5,000 shelters move 6 to 8 million dogs and cats each year through their facilities. Because shelters frequently care for neglected animals with little to no medical history, the prevalence of heartworm disease among these pets is high. Coupled with limited facilities, funding, time, expertise and staffing, the management of heartworm disease becomes a serious challenge for shelters.

Most shelters lack the financial resources to cover the most basic medical care such as vaccinations and spay/neuter surgery, without even considering basic heartworm testing and treatment. As a result, shelter veterinarians and managers often devise compromised heartworm management strategies—or avoid confronting the disease altogether. This can result in less optimal treatment for infected dogs, adoption of infected dogs by the unsuspecting public and an increased risk of heartworm transmission in the community.

Q. What do shelter veterinarians need from organizations such as the American Heartworm Society?

DR. POLAK: The American Heartworm Society (AHS) has issued comprehensive guidelines for the diagnosis, prevention and management of heartworm disease in pets.

“ Many shelters, in fact, lack sufficient funding to cover even the most basic medical provisions... without even considering heartworm testing and treatment. ”

—Dr. Katherine Polak

While these guidelines represent an optimal protocol for testing and treatment, many shelters, especially open-intake shelters, cannot afford to follow them. Shelter veterinarians need information and guidelines tailored to our unique needs. Guidelines should address commonly asked questions by sheltering professionals, including:

- If a shelter can't afford to antigen-test all animals, how can they prioritize resources for testing? What animal populations should they focus on?
- Is there a cheaper way to screen for heartworm than a SNAP test? Also, are some commercially available tests too sensitive for shelter use, and if so, what are the implications of this?
- Should cats be screened for heartworm, and should anything be done if they test positive?
- Can livestock preparations of ivermectin be used as an effective and safe heartworm preventive in the shelter?
- What alternatives do shelters have in terms of shortening pretreatment intervals for infected dogs? Even if a shelter can afford to treat, holding dogs for two to three months during treatment is usually not practical.
- Should heartworm-positive dogs be spayed/neutered before or after treatment?
- What alternatives do shelters have when they can't afford to follow AHS's treatment protocol?

Shelters want to do the right thing and strive to offer communities healthy, adoptable animals. In the case of heartworm, they need more information—and more resources.

JOIN THE AHS COMMUNITY

Heartworm disease is one of the important diseases in companion animals, and it's vital that practitioners stay informed of the latest developments. The best way to do so is to join one—or all—of the AHS communities.



Become an AHS member.

Members receive a number of benefits, from discounts on client education materials and the triennial symposium registration to exclusive materials, such as the AHS symposium proceedings and the quarterly AHS Bulletin. Information on joining is available on heartwormsociety.org/membership/benefits.html



Join the AHS Facebook community.

With nearly 7,000 fans, our Facebook page connects you to the latest information on heartworm, as well as a vital community of veterinary professionals and others who are committed to reducing the incidence of this disease. You can find us at facebook.com/heartwormsociety.



Follow AHS on Twitter.

Follow us on Twitter at [AHS_Think12](https://twitter.com/AHS_Think12), where our community is growing rapidly, and you can link to a wide range of resources and debates. Our Twitter page is also a great place to follow live during AHS symposia.

Both our Facebook and Twitter pages are run by veterinarians who serve on the AHS executive board.



Tune in to AHS on YouTube.

Check out video interviews with speakers from the 2013 Triennial Heartworm Symposium, and download client education videos for use in your practice.

THE AMERICAN HEARTWORM SOCIETY AND YOU

The American Heartworm Society (AHS) is focused on serving the needs of the veterinary profession. Here's how you can take advantage of AHS programs.

HEARTWORM SYMPOSIA

The AHS brings the latest in scientific information to veterinary professionals through scientific symposia. Opportunities include:

- **The Triennial Heartworm Symposium**

This comprehensive conference takes place every three years and includes presentations by leading heartworm experts with attendees from all over the United States and the world. The next symposium will be held in 2016.

- **Conference Symposia**

AHS is sponsoring a half-day symposium for attendees of the North American Veterinary Conference in Orlando, Fla., and the Western Veterinary Conference in Las Vegas, Nev.

- **Heartworm University**

This traveling symposium is a day-long continuing education session offered free of charge to veterinarians and veterinary technicians, and is designed to bring in-depth information on heartworm disease to veterinarians in different locales. Many Heartworm University sessions are held in conjunction with state veterinary medical association meetings.



HEARTWORMSOCIETY.ORG

The American Heartworm Society website is one of the most important resources offered by the AHS. Here, veterinary professionals can access the following:

- **The American Heartworm Society guidelines**, in both comprehensive and summary formats.

- **Heartworm Incidence Maps**, which are based on a triennial nationwide survey of thousands of veterinary practices.

- **The Think 12 Resource Center**, which provides new-client education handouts, videos, infographics, and other materials on heartworm and pet care every month, 12 months a year.



- **Heartworm information**, including FAQs, a video gallery, a glossary of terms and more for both veterinarians and pet owners. In addition, AHS members can access past and present issues of the **AHS Bulletin** and order **client brochures** for their practices.

- **The AHS website** is also a vital resource when challenges arise, whether it's information on lack of efficacy or guidelines for dealing with a product shortfall. In addition, you can learn more on our website about our organization's officers and executive board—all of whom work on a volunteer basis.

HEARTWORM GUIDELINES

The American Heartworm Society is the leading resource on heartworm disease, and the AHS guidelines provide protocols and comprehensive information on prevention, treatment and testing. Because new information is constantly becoming available, these guidelines are updated on an ongoing basis.