

American Heartworm Society

Resistance Statement

Veterinarians rely on macrocyclic lactones (MLs) to protect their patients from heartworm disease, so the evidence from recent research that sub-populations of heartworm have shown resistance to MLs is of great importance in veterinary medicine. Every compound currently marketed in every form of administration (oral, topical, and parenteral) has been shown to be less than perfect in at least one study. However, while the evidence indicates that resistance affects all macrocyclic lactones, differences in active ingredients, doses, and product formulation among the available preventives can result in varying rates of failures.

Research continues in a number of related areas, as scientists strive to understand how heartworm resistance develops, how veterinarians can determine if resistance is an issue in their practice area, and how they can mitigate lack of efficacy in their patients. While there is no definitive test to identify resistant heartworms, a University of Georgia algorithm (see below) that utilizes a microfilarial suppression test can help veterinarians evaluate cases of suspected ML resistance.

It is important that veterinarians understand and communicate this new information about resistance appropriately to pet owners. Key points include:

- Research findings do not demonstrate widespread ineffectiveness of available heartworm preventives; MLs continue to be effective in the vast majority of cases.
- Appropriate, on-label usage of MLs is paramount. Inappropriate product use, such as the use of MLs alone (the "slow-kill" method) to treat heartworm-positive dogs, and the off-label use of large-animal products as heartworm preventives, is not recommended by the American Heartworm Society (AHS).
- Practical mosquito mitigation practices, such as eliminating sources of standing water and keeping pets indoors during peak mosquito times, can help reduce the risk of heartworm transmission. The use of EPA-approved mosquito repellents/ectoparasiticides in conjunction with ML administration can provide more complete protection from resistant as well as susceptible heartworms in highly endemic areas.
- Lack of efficacy in heartworm preventives can be related to many factors, including resistance, but the most important of these is compliance. By following label recommendations for the use of preventives, and monitoring patients appropriately, veterinarians can play a vital role in maintaining the effectiveness of ML medications.

The American Heartworm Society (AHS) guidelines explicitly recommend year-'round administration of ML preventives as well as annual testing. The guidelines also recommend a specific treatment protocol for heartworm-positive dogs. This treatment

protocol includes administration of doxycycline in combination with an ML, followed by a three-dose regimen of melarsomine.

The American Heartworm Society [canine and feline guidelines](#) reflect the latest research presented in this and other scientific forums. The goal of AHS is to continuously provide current and scientifically supported information on heartworm disease, as well as informed guidelines for the veterinary community.



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College of Veterinary Medicine

Updating the diagnostic algorithm for evaluating cases of suspected macrocyclic lactone resistant heartworm infection

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Introduction

The emergence of macrocyclic lactone (ML) resistance in canine heartworm poses a substantial threat to what is currently the only effective, FDA-approved available method of prevention. Further study of the biotypes is necessary to understand the mechanism of resistance and evaluate novel prevention options. Identifying cases of drug-resistant infection remains problematic, however, especially when poor compliance and insufficient testing are concerns. Furthermore, a definitive demonstration of resistance requires experimental infection and treatment, which is prohibitively costly. With the aim of identifying likely cases of macrocyclic lactone-resistant heartworm and preventing their continued spread, we have previously described an algorithm for determining the likelihood of drug resistance and appropriate treatment strategies for each case. This algorithm relied on the microfilarial suppression test (MFST), which has been previously validated as an efficient and discrete measure of the suspected resistance phenotype. However, based on recent findings from the field and novel research projects, we have updated the algorithm, while still maintaining a standardized method and format that is readily available to practitioners.

Node 1

Has the client been compliant with ML administration?

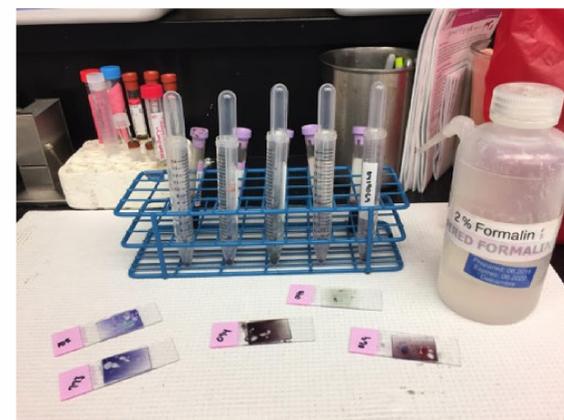
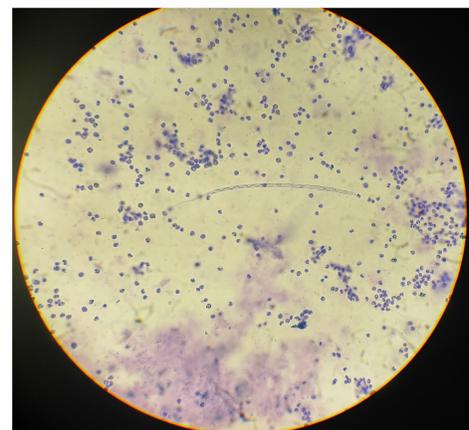
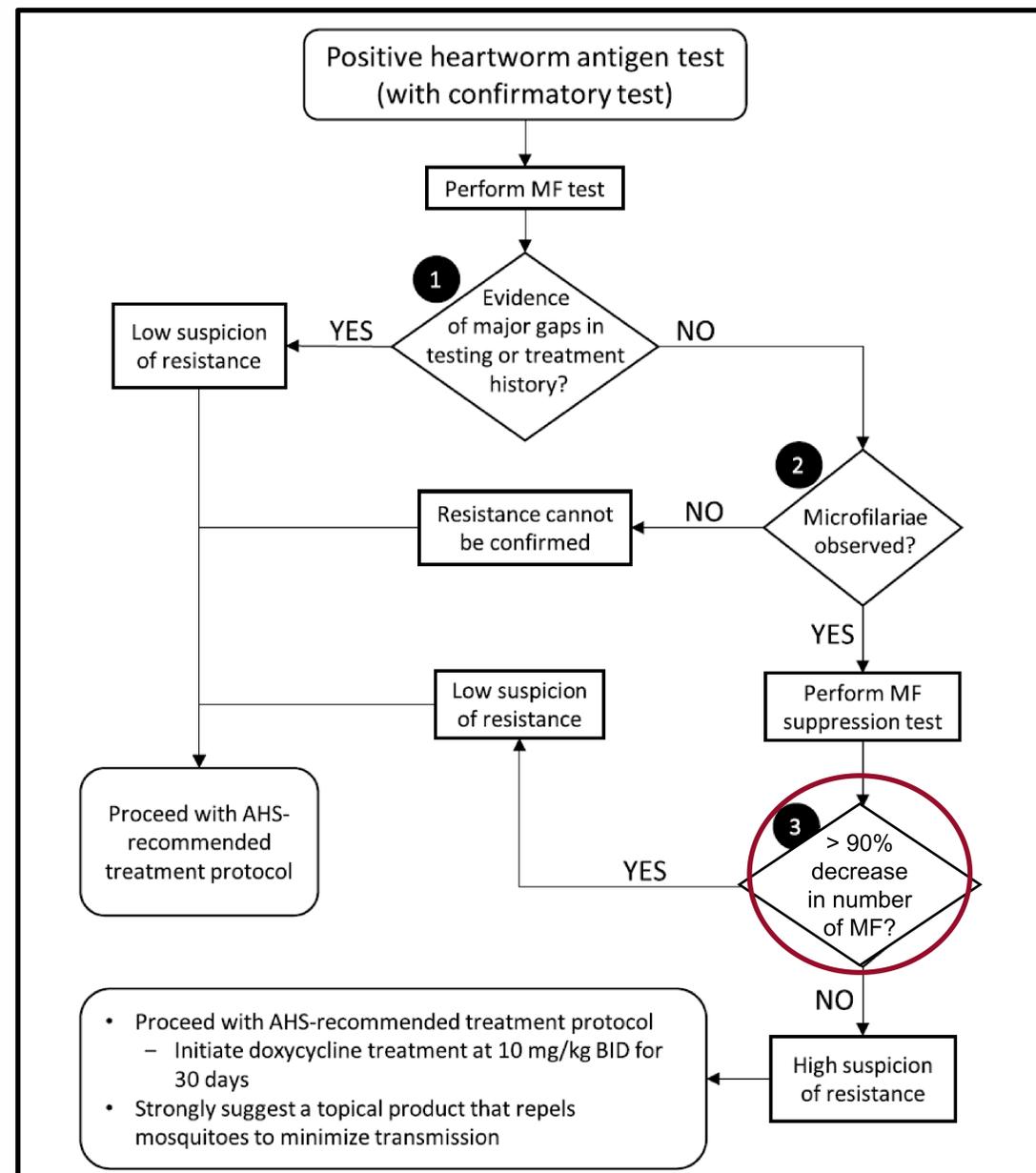
- Review client's purchase history
- Alternatively, veterinarian or staff administer each ML dose
- Careful consideration of dosing band, changes in weight
- Gaps < 2 months, should be investigated thoroughly

Are there gaps in heartworm antigen testing?

- Antigen and microfilariae testing should be done between 6-9 months of age
- Test anytime there is a change in ML drug and 6 months after product switch

Any concurrent medications or illnesses to consider?

Any seasonal ML administration to consider?



Node 2

Have you observed microfilariae on a direct smear or concentration technique?

- If MF are observed, then the MF are persisting in the face of continuous use of ML
- Most previous cases of confirmed resistance maintained a microfilaremia even after the administration of ML at microfilaricidal doses
- Because MF are present, these cases have a high index of suspicion and the MF suppression test should be performed

Make sure to confirm that MF are *Dirofilaria immitis*

Node 3

Run the microfilarial suppression test (MFST)

1. Perform Knott's test for quantitation of MF. The procedure for this test is located at www.heartwormsociety.org. The entire sample should be counted in order to gain the number of MF per milliliter.
2. Administer topical 2.5% moxidectin and 10% imidacloprid (an FDA-approved microfilaricide) after obtaining blood for the Knott's test. The risk of anaphylaxis when 2.5% moxidectin and 10% imidacloprid is administered to a microfilaremic dog is less than ivermectin at 50 µg/kg or milbemycin oxime at 1 mg/kg, however, observation is recommended
3. Perform a second Knott's test for MF quantification 4 weeks after the initial test. The percentage reduction in numbers of MF between the first and second Knott's tests determines whether the case has a high or low suspicion of resistance.
 - i. If there is a > 90% decrease in MF numbers between the two tests, then the suspicion of ML resistance will be low.
 - ii. If there is < 90% reduction, then the index of suspicion will be high.



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