Macroyclic Lactone-Resistant Heartworm Disease

**INITIAL HEARTWORM ANTIGEN TEST PERFORMED**

**Antigen positive**

- **Evidence of poor compliance or lack of prophylaxis**
  - **Dx** Very low suspicion of resistance
  - **Tx** Proceed with American Heartworm Society (AHS)-recommended treatment protocol

- **Gaps present in testing and/or product purchase history?**
  - **Yes**
    - Heartworm antigen test not performed ≥ 6 months after initiation of compliant prophylaxis
      - **Dx** Low suspicion of resistance
      - **Tx** Proceed with American Heartworm Society (AHS)-recommended treatment protocol

    - **INV** Perform MF suppression test:
      - Perform Knott’s test for quantitation of MF
      - Administer ivermectin at 50 μg/kg PO or milbemycin oxime at 1 mg/kg PO—Use a product containing only milbemycin oxime (ie, no combination products)
      - An adverse reaction is unlikely if prophylaxis has been compliant, as previous treatments by the owner would have been made while the dog was microfilaremic; however, because compliance can never be assured, these drugs should be administered at the veterinary hospital and the dog observed for 6 to 8 hours postadministration of microfilaricide
      - Perform a second Knott’s test 7 days after microfilaricide administration

  - **INV** Heartworm antigen test performed ≥ 6 months after initiation of compliant prophylaxis
    - **Yes**
      - Microfilariae (MF) observed?
        - **Yes**
          - Low suspicion of resistance
          - **Tx** Proceed with American Heartworm Society (AHS)-recommended treatment protocol
        - **No**
          - Very low suspicion of resistance
          - **Dx** Resistance can be neither confirmed nor disproven
          - **Dx** Even if resistance is present, further transmission of resistant worms is not possible because MF must be ingested by mosquitoes for parasite transmission to occur
          - **Dx** No special resistance management required
          - **Dx** Proceed with AHS-recommended treatment protocol

- **No**
  - **Dx** High suspicion of resistance
  - **Dx** Immediately initiate doxycycline at 10 mg/kg twice a day for 30 days
  - **Dx** Proceed with AHS-recommended treatment protocol
  - **Dx** Consider a topical product that repels mosquitoes to minimize possibility of transmission

**INV** Gaps present in testing and/or product purchase history?

**INV** Heartworm antigen test not performed ≥ 6 months after initiation of compliant prophylaxis

- **Test necessary to ensure dog was negative at prophylaxis initiation**

**INV** Heartworm antigen test performed ≥ 6 months after initiation of compliant prophylaxis

**INV** Evidence of poor compliance or lack of prophylaxis

**Dx** Very low suspicion of resistance

**Dx** Proceed with American Heartworm Society (AHS)-recommended treatment protocol

**INV** Perform MF suppression test:

- Perform Knott’s test for quantitation of MF
- Administer ivermectin at 50 μg/kg PO or milbemycin oxime at 1 mg/kg PO—Use a product containing only milbemycin oxime (ie, no combination products)
- An adverse reaction is unlikely if prophylaxis has been compliant, as previous treatments by the owner would have been made while the dog was microfilaremic; however, because compliance can never be assured, these drugs should be administered at the veterinary hospital and the dog observed for 6 to 8 hours postadministration of microfilaricide
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**AHS = American Heartworm Society, MF = microfilariae, ML = macrocyclic lactone**
Resistance to macrocyclic lactone (ML) preventives in canine heartworm cases has been proven, though there are few documented cases. To the authors’ best knowledge, clinical patterns to date suggest that most proven cases of ML resistance in heartworms have been diagnosed in dogs residing in or translocated from the Mississippi Delta region and that cases of resistance are rare outside this region. However, it is possible that resistance is more widespread than currently recognized. No tests for resistance are available to determine the prevalence and distribution of resistance in heartworms, making definitive diagnosis impossible.

REFERENCES

ANDY MOORHEAD, DVM, MS, PhD, is a small animal parasitologist at University of Georgia and director of the Filariasis Research Reagent Resource Center. Dr. Moorhead earned his DVM from North Carolina State University and his MS in veterinary parasitology from Purdue University, where he studied the raccoon roundworm Baylisascaris procyonis. He received his PhD in cellular microbiology from Cornell University. Dr. Moorhead’s research interests include the role of host-specific cues in development of filarial worms, specifically Dirofilaria immitis and Brugia malayi.

RAY M. KAPLAN, DVM, PhD, DEVPC, DACVM (Parasitology), is a professor of parasitology and director of the Parasitology Diagnostic Laboratory at University of Georgia, as well as past president of the American Association of Veterinary Parasitologists (2015-2016). He earned his DVM from Virginia-Maryland Regional College of Veterinary Medicine and his PhD in veterinary parasitology at University of Florida. Dr. Kaplan’s research program is focused on measuring, understanding, and solving drug resistance in nematode parasites.

* Performance of the MF suppression test is recommended by the authors solely to identify resistant heartworm cases and is not a normal standard of care procedure for treating heartworm cases.
† To the authors’ knowledge, all proven cases of resistance to date have been microfilaricidal. Lack of MF suggests that the case does not involve resistance, the dog has no female worms, or infections are still immature and have not yet become patent.