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Peer Reviewed

Canine Heartworm: ***Positive Result Despite Prevention***

A 9-month-old Labrador retriever presents to your practice in upstate New York in October.

History. The owner recently adopted the pet from the local community shelter. The dog is happy and healthy, although slightly underweight.

Physical Examination. Findings on the physical examination are normal.

Diagnostics. The fecal test result is positive for roundworms and tapeworms. The result of a heartworm antigen test is negative. The dog is treated with Drontal Plus (bayerdvm.com) to clear its tapeworm and roundworm infection.

Follow-Up & Additional Diagnostics. In March of the next year, the dog is examined at a 6-month checkup and begins receiving a 6-month course of heartworm preventive agent. The prevention regimen continues through October. The following March, the dog is positive for heartworms on the antigen detection test and has circulating microfilariae in the blood.

CONTINUES

ASK YOURSELF ...

- What is missing from the management plan?
- What additional protection should the client receive relative to any guarantee associated with the product?
- What are the possible causes of lack of efficacy reported for heartworm preventive agents?

CONSIDER THIS

Consider the following scenario: Preventive treatment is stopped in October, infection occurs in November, and the dog is retested in April (5 months after infection) and begins receiving preventive therapy. This therapy continues for 6 or 7 months and is discontinued in October (assuming that the mosquitoes that year stop activity at the usual time in September), and the infection is not noted until the following April. Infection might be detected earlier than that if signs develop.

DIAGNOSIS:
This case may represent a loss of efficacy, or it may be a preexisting infection. Could this be a case of resistance?

Dogs receiving preventive therapy for heartworms should remain heartworm-negative. This is the point of a daily prevention regimen, or for using a product monthly or every 6 months. The premise that the preventive agent will protect is based on 3 basic assumptions:

1. That the product administered is what the manufacturer says it is and has not been tainted by a manufacturing or storage glitch.
2. That the product has been properly administered without any breaks in treatment.
3. That the dog was not infected with advanced-stage larvae or prepatent adults at the time of administration.

Fortunately, in the United States we have fairly good safeguards against counterfeit product, and government agencies and manufacturers do what they can to ensure that all batches meet quality assurance standards.

The assumption that the product was properly administered is verified by purchase records and faith or trust, unless the product was the 6-month injectable formulation administered by a practitioner; then, the only real variable is proper pretreatment mixing of the vial contents. With all products, there is always concern that dogs may grow out of the administered dose band; however, as long as veterinarians discuss this with the client, this problem should not be a real concern.

The final assumption is that the dog was not infected at the time of initiation of preventive treatment. In a dog under 6 months of age or a new canine patient over 6 months, the safest thing to do is to check the dog again 4 or so months after treatment. This is sufficient time for most 2-month-old larvae, which are more resilient to macrocyclic lactone therapy than younger larvae, to develop to the adult stage and produce antigen for detection on a heartworm test. (Only females produce antigen, so all-male infections would go undetected.)

Follow-Up Testing. Follow-up antigen testing is necessary because you do not know where a dog

What Can We Learn From This Case?

This dog was probably infected in the late summer of its first year of life. Regardless of whether the dog had begun receiving heartworm prevention at the time of its first visit, the dog should have undergone antigen testing 4 months after starting its preventive regimen.

over 6 months of age may have lived before coming to the clinic. Even in March in Hamilton, Ontario, Canada, a 9- or 10-month-old dog from a shelter could have spent the previous summer somewhere south where heartworms abound. When dealing with preventive agents, you need to err on the side of caution; if you do not know the dog's history and the dog is over 6 months old, perform an antigen test before starting preventive therapy and a second test 4 to 6 months afterward.

Year-Round Prevention. If dogs are not receiving year-round prevention, it is much more difficult to determine whether one is dealing with lack of efficacy or an infection present before the commencement of prevention. I firmly favor year-round heartworm prevention with internal and external parasite control throughout the United States. However, others feel differently, and the scenario described earlier becomes more complicated to interpret when the choice has been made not to use year-round therapy.

It takes 6 months, more or less, for a dog to develop an infection that is detectable by an antigen test. For example, say that a dog starts prevention 2 months later than it should (eg, if the mosquito season is early or the client is slow to get started in the spring). After 6 months of treatment, because of the resilient 2-month-old larvae present at the commencement of the preventive therapy, the dog can be positive when tested before the next spring's annual check.

CONTINUES

? DID YOU ANSWER?

- **What is missing:** The second antigen test 4 months after the animal begins receiving preventive therapy.
- **Additional protection relative to the guarantee:** Many product guarantee programs clearly spell out when testing is to be performed before and after treatment begins and when products are switched. It is important that these guidelines from the manufacturer be followed to protect the client. These guarantees are probably not upheld if the veterinarian is uncertain that the source from which the product was purchased performs appropriate testing and records the results.
- **Causes of lack of efficacy:** Most losses of efficacy are probably due to infections that exist before the start of preventive therapy. However, in some cases, the product has not worked as well as was expected; thus, the FDA believes it is incorrect to label all products as 100% efficacious in preventing infection. In parts of Louisiana, Arkansas, and Mississippi, some practitioners firmly believe they see far too many losses of efficacy in patients where they are certain the owners are fastidious in their adherence. Is this resistance? People are working very hard to try and unravel this well-knotted question.

This case probably represents an unlucky dog and unfortunate timing of events relative to acquisition of infection. The dog was infected with young worms that first October, and the infection was still not patent for detectable antigen the next March. The dog began receiving a preventive regimen, but the worms were too large and robust to be killed with the macrocyclic lactone.

Only after another year was a second test done to detect mature worms that could probably have been diagnosed the previous June.

Of course, this scenario would become much harder to interpret in an area where people are becoming convinced that infective larvae can develop even in dogs that are receiving monthly prevention.

READ MORE

Is it Resistance? An Evidence-Based Inquiry
Proceedings of the 13th Triennial State of the Heartworm Symposium 2010, pages 10-11
Available at **heartwormsociety.org**

Year-Round Heartworm Prevention: Two Viewpoints
Clinician's Brief, April 2009, pages 25-27
Available at **cliniciansbrief.com**

Along the same line, if prevention is stopped too soon, the dog can become infected after therapy is stopped. In this scenario, the worms might be detected the next spring, but it is just as likely that they are still too young to be making antigen. Because the macrocyclic lactones do not kill adult worms rapidly, it might be 18 months before the infection is detected (see **Consider This**).

When dogs receive preventive therapy only a portion of the year, clinicians will find it more difficult to determine whether the infection is due to a problem with the product or has resulted from mistaken judgment about when to start or stop treatment.

Efficacy. Loss of efficacy related to product attributes has been reported, and the FDA has warned that not all products may be providing 100% protection against infection.

For example, a topical product was found not to be 100% efficacious, apparently as a result of some problems with skin absorption. The data on various additional tests were carefully examined by the corporation and the FDA, and every veterinarian in the United States received a letter stating that the product was not claiming 100% efficacy. However, there was a sense that loss of efficacy was increasingly being reported to the FDA at that time.

Reasons for this perception included practitioners' close scrutiny of new products entering the market and their tendency to call in failures, changes in recording methods required by the FDA, and perhaps an actual increase in loss of efficacy. As a result, it was suggested to the manufacturers of heartworm products that they should no longer claim the products are 100% effective. This is basically where the situation now stands.

Possibility of Resistance. There are rumors that along portions of the Mississippi River and parts of the Mississippi Delta region, more losses of efficacy are occurring than elsewhere in the United States. Of course, practitioners facing an uncomfortable number of losses of efficacy may wonder whether these losses are caused by the worms' resistance to the products.

Practitioners and clients claim that they are seeing significant product failure among large-breed rural dogs that live mainly outside. In addition, throughout the United States and in Canada, practitioners and parasitologists have observed dogs treated for adult heartworms that still have circulating microfilariae after converting to a negative antigen status and receiving monthly prophylaxis for several months.

Many scenarios are being posited to explain current observations relative to heartworms, such as persistent microfilariae following monthly preventive administration postadulticide treatment and the worrisome infections along the Mississippi River. People are looking closely at this situation and data on the topic was presented at the American Heartworm Society's Thirteenth Triennial Symposium in April. The Companion Animal Parasite Council (CAPC) and the AHS are holding a joint roundtable at the end of August to discuss some of these issues, the data behind them, how best to monitor what is occurring, and how to respond to veterinarians' concerns about the current state of heartworm prevention.

RESOURCES

American Heartworm Society: **heartwormsociety.org**

Companion Animal Parasite Council: **capcvet.org**

Heartworm—Prevention, Infection, & Treatment (interactive training CD): **lifelearn.com**