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Heartworm 'lack of effectiveness' claims in the Mississippi delta: Computerized analysis of owner compliance – 2004–2011

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ABSTRACT

A retrospective medical record review was conducted to identify factors from veterinary clinic medical records that may have contributed to suspected ineffectiveness of a heartworm preventive product. Patient records of 271 dogs, comprising 301 instances of positive heartworm antigen test results while the dogs were receiving heartworm preventive were evaluated. Nineteen veterinary practices in 17 counties and parishes in Arkansas, Louisiana, Mississippi, and Tennessee participated in the study. Records were selected by the veterinary clinics as representative of cases of suspected lack of effectiveness for a heartworm preventive, and for which an owner satisfaction claim had been filed with the manufacturer. Medical record data were entered into a software program, and a graphic representation was created to facilitate analysis of whether pet owners had purchased sufficient heartworm preventive for the dog to be compliant during the period when infection with *Dirofilaria immitis* could have led to the positive heartworm antigen test result for that patient ("window of infection"). In 243 (80.7%) cases, there was insufficient heartworm preventive purchased, leading to a gap in protection during the "window of infection". In only five cases (1.7%) there were no purchase lapses or extenuating circumstances (underdosing of medication, multiple purchase gaps outside the established window of infection, or dogs have been diagnosed with heartworm infection more than once during the period studied). Half the cases were from multiple-dog households, and in many of these households, sharing of product between pets was acknowledged. In another 28% of the cases from multiple-dog households, more product was purchased than was needed for one dog, suggesting that the product was being shared between more than one pet. In most cases, there was at least one reason that a dog did not receive sufficient heartworm preventive product, placing the dog at risk of developing an infection with mature heartworms. Several actions were identified that veterinary clinics can take to improve heartworm disease prevention in their patients.

1. Introduction

Heartworm preventive medications belong to the macrocyclic lactone class of drugs and are indicated for the prevention of heartworm disease. Most products are

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designed for monthly use, and product labels include language that links the administration of product to the animal being exposed to mosquitoes. Both the American Heartworm Society and the Companion Animal Parasite Council recommend year-round administration of heartworm preventives (American Heartworm Society, 2009; Companion Animal Parasite Council, 2013), largely because attempting to time the administration of heartworm preventive medication precisely to mosquito risk is impractical and may permit a larval infection to mature to the adult stage.

In recent years, some veterinarians practicing in a region of the United States comprising areas of Arkansas, western Tennessee, Mississippi, and Louisiana (referred together as the Mississippi Delta, or the Delta) have reported an increasing number of cases of dogs that tested heartworm antigen positive while receiving heartworm preventive medication (Hartogenis, 2005). The reports have led to speculation that *Dirofilaria immitis* has developed selectional resistance to heartworm preventives (American Heartworm Society, 2010).

In recently reported studies, isolates of *D. immitis* with less than 100% susceptibility to heartworm preventive products in an induced heartworm infection model have been identified (Blagburn et al., 2013a,b). The relevance of these findings to field cases of suspected lack of heartworm preventive efficacy has not been determined, but the risk of selecting for *D. immitis* genotypes that confer reduced susceptibility, particularly by repeated administration of macrocyclic lactone products to dogs with patent heartworm infections, has been identified (Pulaski et al., 2013).

There are many reasons that a dog might test positive for circulating *D. immitis* antigen while on a heartworm preventive. The relationship between the heartworm lifecycle and the timing of testing and even the effect that heartworm preventives may have on antigen release by mature heartworms can affect testing outcomes and give the false impression that a particular product "failed" (American Heartworm Society, 2009). However, experts agree that most such cases are probably the result of a failure of pet owners to give heartworm preventive according to the product label, allowing larval stages of *D. immitis* to mature into adult worms (Cummings et al., 1995; Bowman and Atkins, 2009; American Heartworm Society, 2010, 2012; Companion Animal Parasite Council, 2013). Nonetheless, some veterinarians practicing in the Delta insist that they have seen an increasing number of cases in which they were certain that owners were compliant in purchasing and administering heartworm preventive and yet dogs still tested heartworm antigen positive (Bourguinat et al., 2011; Geary et al., 2011).

Heartworm preventive manufacturers offer customer satisfaction programs, often referred to as "guarantees", that provide different levels of support to veterinarians for the treatment of dogs that test positive for circulating heartworm antigen and for which heartworm preventive product was dispensed to the pet owner. Criteria for obtaining assistance and the levels of support vary by manufacturer but generally require that a dog be treated with the manufacturer's heartworm preventive product during the previous year and that the dog have a prior negative antigen test. Provision of assistance does not indicate that a product failed, but all cases describing a suspected lack of expected effect submitted to manufacturers must be reported to regulatory authorities, according to local regulatory requirements. For example, in the United States, these cases are reported to the Food and Drug Administration, Center for Veterinary Medicine (FDA CVM) as suspected adverse drug events (coded as INEFFECT, HW LARVAE).

The study reported here was conducted to determine whether sufficient heartworm preventive product was available to dogs for which product failure was suspected and to identify factors from the medical records that may have contributed to these dogs testing heartworm antigen positive. Indeed, the results of the study reported herein strongly indicate that the vast majority of lack of expected effects are associated with failure of dog owners to purchase adequate product to meet recommendations for heartworm prevention. Characterizing factors that the veterinary practice or pet owners can control may lead to actions that can reduce the number of dogs developing heartworm disease.

2. Materials and methods

2.1. Case selection

Patient case records from veterinary practices were reviewed. The principal investigator visited 19 veterinary practices in 17 counties and parishes in Arkansas, Louisiana, Mississippi, and Tennessee. Clinics were selected on the basis of having submitted heartworm preventive guarantee claims, willingness to provide records to the investigator, dispensed more than one heartworm preventive product, and perceived that they had a lack of expected effect of heartworm preventives in some of their patients.

The veterinary practices selected the patient records to be reviewed and chose cases that they considered to represent lack of expected effect. These cases were those that had been submitted to a manufacturer for assistance and for which the clinic believed that the dog had received the recommended heartworm preventive medication, which for all clinics was every month, year-round.

2.2. Data collection

Information was taken from patient charts and practice management transaction records. Records of other dogs in the household were reviewed when indicated (e.g., when there were unusual purchase histories in the medical record of the dog of note, suggesting the possibility of product sharing; when multiple dogs shared the same paper medical record; when there were long lapses in preventive purchase that could have been negated by purchase on another dog's record; when the paper medical record indicated that a purchase was for more than one dog). Additionally, prescriptions for internet purchases were sought out and taken into account. Data were entered into a computerized form (FLASH® CS3, Adobe Systems Incorporated, San Jose, CA) linked to software application, the window of infection (WOI) tool (www.heartwormedu.com).