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# Seroprevalence of heartworm infection, risk factors for seropositivity, and frequency of prescribing heartworm preventives for cats in the United States and Canada

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## OBJECTIVE

To determine the seroprevalence of heartworm infection, risk factors for seropositivity, and frequency of prescribing heartworm preventives for cats.

## DESIGN

Prospective cross-sectional study.

## ANIMALS

34,975 cats from 1,353 veterinary clinics ( $n = 26,707$ ) and 125 animal shelters (8,268) in the United States and Canada.

## PROCEDURES

Blood samples were collected from all cats and tested with a point-of-care ELISA for *Dirofilaria immitis* antigen, FeLV antigen, and FIV antibody. Results were compared among geographic regions and various cat groupings.

## RESULTS

Seropositivity for heartworm antigen in cats was identified in 35 states but not in Canada; overall seroprevalence in the United States was 0.4%. Seroprevalence of heartworm infection was highest in the southern United States. A 3-fold increase in the proportion of seropositive cats was identified for those with (vs without) outdoor access, and a 2.5-fold increase was identified for cats that were unhealthy (vs healthy) when tested. Seroprevalence was 0.3% in healthy cats, 0.7% in cats with oral disease, 0.9% in cats with abscesses or bite wounds, and 1.0% in cats with respiratory disease. Coinfection with a retrovirus increased the risk of heartworm infection. Heartworm preventives were prescribed for only 12.6% of cats at testing, and prescribing was more common in regions with a higher seroprevalence.

## CONCLUSIONS AND CLINICAL RELEVANCE

At an estimated prevalence of 0.4%, hundreds of thousands of cats in the United States are likely infected with heartworms. Given the difficulty in diagnosing infection at all clinically relevant parasite stages and lack of curative treatment options, efforts should be increased to ensure all cats receive heartworm preventives. (*J Am Vet Med Assoc* 2017;250:873–880)

Cats are at risk for infection with the agent of heartworm disease, *Dirofilaria immitis*, whenever infected dogs exist.<sup>1</sup> Most cats are capable of eliminating heartworms before the parasites reach the mature adult stage detectable by antigen tests; however, they are still susceptible to chronic heartworm-associated respiratory disease induced by immature heartworms. Such cats may have positive results of heartworm antibody testing or may escape detection altogether.

The most common clinical signs of infection in cats involve the respiratory system, with coughing, tachypnea, dyspnea, and increased bronchovesicular sounds similar to those in cats with asthma.<sup>1</sup> Infected cats may have vomiting or neurologic signs. In some situations, sudden death is the first indication

of infection. In contrast to dogs, curative treatment is not safe or practical for cats, so treatment is aimed at palliation of clinical signs. Whereas diagnosis and treatment of heartworm infection in cats can be challenging, heartworm preventives are safe and highly effective.

A suggested method for estimating the local prevalence of heartworm infection in cats when feline-specific data are unavailable is to calculate 5% to 20% of the regional heartworm infection rate for unprotected dogs.<sup>2–4</sup> Over the past 27 years, necropsy studies<sup>3,5–10</sup> involving a total of 2,360 southeastern US shelter cats have collectively led to the identification of adult heartworms in 115 cats, for an overall prevalence of 4.9%, but less information is available regarding the prevalence of infection in owned cats, particularly in those with no clinical signs. The purpose of the study reported here was to estimate the seroprevalence of and risk factors for heartworm infection in owned cats in the United States and Canada and

## ABBREVIATIONS

CI Confidence interval

to determine the frequency with which heartworm preventives were prescribed for cats.

## Materials and Methods

### Participant selection

Veterinary clinics and animal shelters in the United States (excluding the territories) and Canada were

invited to participate in the study through a letter addressed to purchasers of diagnostic test kits (IDEXX customers), animal shelters listed in web directories, members of the American Association of Feline Practitioners, and members of the Association of Shelter Veterinarians. Facilities were eligible to participate if they performed a monthly minimum of 25 point-

**Table 1**—Results of bivariate analyses of putative risk factors for heartworm seropositivity in 34,975 adult cats tested at 1,353 veterinary clinics (n = 26,707) and 125 animal shelters (8,268) in the United States (excluding the territories) and Canada from March to September 2010.

Factor	Category	No. of cats tested	No. of cats with positive results	Seroprevalence (%)	OR	95% CI	P value
Test site	Animal shelter	8,268	31	0.4	Referent	—	—
	Veterinary clinic	26,707	110	0.4	1.1	0.7–1.6	0.60
Geodivision	Canada	409	0	0.0	NA	NA	NA
	Mid-Atlantic	5,299	5	0.1	Referent	—	—
	Mountain	1,011	1	0.1	1.1	0.1–9.0	1.00
	New England	2,917	7	0.2	2.6	0.8–8.0	0.10
	East north central	6,506	21	0.3	3.4	1.3–9.1	0.01
	Pacific	3,330	11	0.3	3.5	1.2–10.1	0.02
	East south central	1,807	8	0.4	4.7	1.5–14.4	0.007
	West north central	3,268	15	0.5	4.9	1.8–13.4	0.002
	South Atlantic	7,564	51	0.7	7.2	2.9–18.0	< 0.001
	West south central	2,864	22	0.8	8.2	3.1–21.7	< 0.001
Sex	Female	17,333	62	0.4	Referent	—	—
	Male	17,642	79	0.4	1.3	0.9–1.8	0.19
Neuter status (excluding unknowns)	Castrated male	12,323	39	0.3	Referent	—	—
	Spayed female	10,558	35	0.3	1.1	0.7–1.7	0.84
	Sexually intact female	6,213	24	0.4	1.2	0.7–2.0	0.44
	Sexually intact male	5,110	40	0.8	2.5	1.6–3.9	< 0.001
Outdoor access	No	12,613	21	0.2	Referent	—	—
	Yes	22,362	120	0.5	3.2	2.0–5.2	< 0.001
Owned	Yes	23,288	85	0.4	Referent	—	—
	No	11,687	56	0.5	1.3	0.9–1.8	0.10
Duration of ownership (owned cats only)	> 30 d	17,869	63	0.4	Referent	—	—
	≤ 30 d	5,419	22	0.4	1.2	0.7–1.9	0.60
Unowned status	Relinquished	3,303	9	0.3	Referent	—	—
	Feral	1,372	7	0.5	1.9	0.7–5.1	0.20
	Stray	7,012	40	0.6	2.1	1.0–4.3	0.04
Test reason (clinic only)	Recheck	3,367	7	0.2	Referent	—	—
	New pet	6,285	18	0.3	1.4	0.6–3.3	0.50
	At risk	6,066	19	0.3	1.5	0.6–3.6	0.90
	Sick	7,570	41	0.5	2.6	1.2–5.8	0.02
Health status	Healthy	21,991	57	0.3	Referent	—	—
	Other	6,824	28	0.4	1.6	1.0–2.5	0.05
	Oral disease	1,507	11	0.7	2.8	1.5–5.4	0.002
	Abscess or bite wound	1,742	15	0.9	3.3	1.9–5.9	< 0.001
	Respiratory	2,911	30	1.0	4.0	2.6–6.3	< 0.001
Coinfection	None	32,065	100	0.3	Referent	—	—
	FeLV	1,102	7	0.6	2.0	1.0–4.4	0.07
	FIV	1,632	21	1.3	4.2	2.6–6.7	< 0.001
	FeLV and FIV	176	13	7.4	25.5	14.0–46.4	< 0.001
Heartworm preventive prescribed	No	30,567	117	0.4	Referent	—	—
	Yes	4,408	24	0.5	1.4	0.9–2.2	0.10

— = Not calculated. NA = Not applicable (Canada had no seropositive cats).

Testing was performed by use of a point-of-care ELISA designed to detect heartworm antigen, FeLV antigen, and FIV antibody in blood, plasma, or serum samples. Values of  $P < 0.05$  were considered significant.

of-care tests for heartworm, FeLV, and FIV infection. Facilities were provided with a data-reporting form and a copy of the American Heartworm Society guidelines for heartworm management in cats, which recommend testing to confirm a diagnosis on the basis of clinical suspicion, to monitor infection status in cats in which heartworm infection had already been diagnosed, and to determine infection status prior to starting heartworm preventive administration.<sup>1</sup> For a companion study on FeLV and FIV seroprevalence, they also received a copy of the American Association of Feline Practitioners retrovirus management guidelines, which recommend testing ill cats, cats with a suspected or unknown exposure history, cats about to be vaccinated against FeLV or FIV, and new pets.<sup>11</sup>

## Data collection

Over a 7-month period (March to September 2010), staff members at clinics and shelters that agreed to participate were asked to perform serologic testing and record the results, as well as data regarding cat signalment and health status, on a standardized data-reporting form. Only veterinary clinic personnel reported the reasons cats were selected for testing because animal shelters typically have blanket policies for infectious disease testing and not protocols based on risk assessment for individual animals. For ease of survey completion, participants were asked to report whether they had prescribed a heartworm preventive at the time of testing, but they were not required to report whether cats had previous prescriptions for a heartworm preventive. Completed forms were sent to study investigators by facsimile transmission.

## Testing protocol

All tests were performed with a commercially available point-of-care ELISA test kit<sup>a</sup> for heartworm antigen, FeLV antigen, and FIV antibody detection in blood, serum, or plasma samples. Reported sensitivity and specificity of the test were 86.7% and 100%, respectively, for detection of heartworm antigen; 100% and 98.6%, respectively, for detection of FeLV antigen; and 99.2% and 100%, respectively, for detection of FIV antibody.<sup>b</sup> Confirmatory testing was not included in the study.

## Risk factor identification

Information collected on the data-reporting form included age (juvenile [ $\leq 6$  months] or adult [ $> 6$  months]; only cats  $> 6$  months were included in the study), sex and neuter status, test results, whether a heartworm preventive was prescribed at the time of testing (yes or no), outdoor access (yes or no), ownership duration ( $\leq 30$  days or  $> 30$  days) or unowned status (stray,

feral, or owner relinquished), reason for testing (new pet, at risk for infection, illness, or recheck), and current health status. Health status options included healthy, respiratory disease, oral disease, abscess or bite wound, and a free-text entry space for other conditions. Geographic region of testing was determined by the location of the veterinary clinic or animal shelter where testing was performed. These locations were grouped by US Census Bureau divisions (geodivisions) as follows: mid-Atlantic (New Jersey, New York, and Pennsylvania), mountain (Arizona, Colorado, Idaho, Montana, New Mexico, Nevada, Utah, and Wyoming), New England (Connecticut, Massachusetts, Maine, New Hampshire, Rhode Island, and Vermont), east north central (Illinois, Indiana, Ohio, Michigan, and Wisconsin), Pacific (Alaska, California, Hawaii, Oregon, and Washington), east south central (Alabama, Kentucky, Mississippi, and Tennessee), west north central (Iowa, Kansas, Minnesota, Missouri, North Dakota, Nebraska, and South Dakota), south Atlantic (Delaware; Florida; Georgia; Maryland; North Carolina; South Carolina; Virginia; Washington, DC; and West Virginia), and west south central (Arkansas, Louisiana, Oklahoma, and Texas). Canada was treated as a separate geodivision.

## Statistical analysis

Because detectable heartworm antigen only develops in mature worms that are at least 6 months of age, results from cats  $\leq 6$  months of age were excluded from the analysis. Seroprevalence was defined as the percentage of cats with positive ELISA results for heartworm antigen. Unadjusted estimates of heartworm seroprevalence and their 95% CIs were calculated by use of the modified Wald method. Asymptotic  $\chi^2$  tests were used to test for bivariate associations between each of the putative risk factors and seropositivity. Crude (unadjusted) ORs and their 95% CIs were calculated. All statistical analyses were



**Figure 1**—Zip-code locations of veterinary clinics or animal shelters at which 141 cats were seropositive for heartworm infection from March to September 2010. A total of 34,566 cats were tested by use of a point-of-care ELISA at 1,333 veterinary clinics ( $n = 26,441$ ) and 121 animal shelters (8,125) in the United States, for an overall seroprevalence of 0.4%.

performed with standard software.<sup>c-c</sup> Values of  $P < 0.05$  were considered significant.

## Results

A total of 1,333 veterinary clinics (26,441 cats) and 121 animal shelters (8,125 cats) in the United

States participated in the study and submitted complete information regarding 34,566 adult cats from all 50 states. A total of 20 veterinary clinics (266 cats) and 4 animal shelters (143 cats) in Canada submitted test results from 409 adult cats from 7 of 10 Canadian provinces (British Columbia, Alberta, Saskatchewan,

**Table 2**—Seroprevalence of heartworm infection by state in 34,566 cats tested by use of a point-of-care ELISA at 1,333 veterinary clinics ( $n = 26,441$ ) and 121 animal shelters (8,125) across the United States from March to September 2010.

State	No. of cats tested	No. of cats with positive results	Seroprevalence (%)	95% CI (%)
Kansas	439	7	1.6	0.7–3.3
Georgia	1,343	16	1.2	0.7–1.9
Hawaii	85	1	1.2	0.0–7.0
Louisiana	345	4	1.2	0.3–3.1
Alabama	96	1	1.0	0.0–6.2
South Carolina	390	4	1.0	0.3–2.7
Texas	1,449	12	0.8	0.5–1.5
Arkansas	503	4	0.8	0.2–2.1
Florida	2,016	16	0.8	0.5–1.3
Oregon	701	5	0.7	0.3–1.7
North Carolina	1,422	10	0.7	0.4–1.3
Missouri	1,021	6	0.6	0.2–1.3
Mississippi	344	2	0.6	0.0–2.2
Vermont	176	1	0.6	0.0–3.5
Michigan	1,709	7	0.4	0.2–0.9
Tennessee	759	3	0.4	0.1–1.2
Ohio	1,579	6	0.4	0.2–0.9
Colorado	270	1	0.4	0.0–2.3
Illinois	558	2	0.4	0.0–1.4
Washington	282	1	0.4	0.0–2.2
Oklahoma	567	2	0.4	0.0–1.4
Kentucky	608	2	0.3	0.0–1.3
Virginia	1,220	4	0.3	0.1–0.9
Maine	957	3	0.3	0.1–1.4
Indiana	1,444	4	0.3	0.1–0.7
Connecticut	526	1	0.2	0.0–1.2
California	2,244	4	0.2	0.1–0.5
New Hampshire	567	1	0.2	0.0–1.1
Minnesota	1,166	2	0.2	0.0–0.7
Wisconsin	1,216	2	0.2	0.0–0.6
Massachusetts	625	1	0.2	0.0–1.0
New Jersey	894	1	0.1	0.0–0.7
New York	2,013	2	0.1	0.0–0.4
Maryland	1,033	1	0.1	0.0–0.6
Pennsylvania	2,392	2	0.1	0.0–0.3
Alaska	18	0	0.0	0.0–20.7
Arizona	285	0	0.0	0.0–1.6
Delaware	27	0	0.0	0.0–14.8
Iowa	385	0	0.0	0.0–1.2
Idaho	74	0	0.0	0.0–5.9
Montana	18	0	0.0	0.0–20.7
North Dakota	90	0	0.0	0.0–4.9
Nebraska	90	0	0.0	0.0–4.9
New Mexico	86	0	0.0	0.0–5.1
Nevada	25	0	0.0	0.0–15.8
Rhode Island	66	0	0.0	0.0–6.6
South Dakota	77	0	0.0	0.0–5.7
Utah	126	0	0.0	0.0–3.6
West Virginia	113	0	0.0	0.0–4.0
Wyoming	127	0	0.0	0.0–3.5



**Table 3**—Proportions of cats in Table 1 for which heartworm preventives were prescribed at the time of heartworm testing.

Geodivision	No. of cats tested	Heartworm seroprevalence (%)	No. of cats with preventive prescribed	Percentage of cats with preventive prescribed	OR for preventive prescribed	95% CI	P value
Canada	409	0.0	12	2.9	Referent	—	—
Pacific	3,330	0.3	156	4.7	1.6	0.9–3.0	0.11
Mountain	1,011	0.1	62	6.1	2.2	1.2–4.1	0.02
Mid-Atlantic	5,299	0.1	400	7.5	2.7	1.5–4.8	< 0.001
New England	2,917	0.2	233	8.0	2.9	1.6–5.2	< 0.001
West north central	3,268	0.5	363	11.1	4.1	2.3–7.4	< 0.001
East south central	1,807	0.4	219	12.1	4.6	2.5–8.2	< 0.001
West south central	2,864	0.8	412	14.4	5.6	3.1–10.0	< 0.001
South Atlantic	7,564	0.7	1,301	17.2	6.9	3.9–12.2	< 0.001
East north central	6,506	0.3	1,250	19.2	7.9	4.4–14.0	< 0.001

See Table 1 for key.

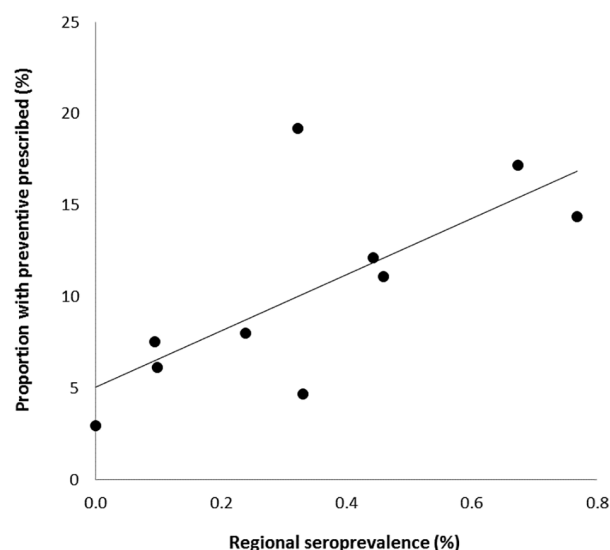
Manitoba, Ontario, Quebec, and Nova Scotia). Overall, 26,707 cats were tested at veterinary clinics, and 8,268 cats were tested at animal shelters.

Of the 26,707 cats tested in veterinary clinics, 7,570 (28.3%) were tested because of current illness; 6,285 (23.5%) were tested as part of a new pet examination; 6,066 (22.7%) were tested because they were perceived to be at risk for heartworm, FeLV, or FIV infection; and 3,367 (12.6%) were having a recheck test.

One hundred forty-one (0.4%) cats were seropositive for heartworm antigen. No cats were seropositive in Canada. A high proportion of seropositive cats ( $n = 120$  [85.1%]) had outdoor exposure. In addition, more than half of seropositive cats were reported to have illness (84 [59.6%]) or retroviral infection (41 [29.1%]).

Risk factors identified through bivariate analysis as significantly associated with seropositivity for heartworm antigen included outdoor access (vs no outdoor access), sexually intact males (vs castrated males), and clinical disease or retroviral infection (vs no disease or infection; **Table 1**). Without controlling for other factors, unhealthy cats had a 2.5-fold increased risk of seropositivity, compared with the risk for healthy cats (OR, 2.5; 95% CI, 1.8 to 3.5;  $P < 0.001$ ). Specific health conditions associated with an increased risk of seropositivity relative to that for healthy cats included abscess or bite wound, oral disease, and respiratory disease. The greatest risk factor for seropositivity for heartworm antigen was simultaneous seropositivity for retroviral antibody or antigen. Seropositivity for antigen or antibody against 1 retrovirus increased the risk of seropositivity for heartworm antigen 2- to 4-fold, whereas seropositivity for antigen or antibody against both retroviruses increased the risk of heartworm seropositivity approximately 25-fold.

Although cats were seropositive in 35 of 50 US states, seroprevalence had a highly regional distribution (**Figure 1**; **Table 2**). Seroprevalence was highest in several southern (west south central, east south central, and south Atlantic divisions) and Midwestern (west north central division) regions and lowest in several northeastern (middle Atlantic and New England divisions) and western (mountain division) regions.



**Figure 2**—Correlation between regional (geodivision) heartworm seroprevalence and proportions of cats for which heartworm preventive was prescribed at the time of heartworm testing (correlation coefficient, 0.7;  $P = 0.03$ ). A total of 34,975 cats were tested by use of a point-of-care ELISA at 1,353 veterinary clinics ( $n = 26,707$ ) and 125 animal shelters (8,268) in the United States (excluding the territories) and Canada.

Overall, heartworm preventives were prescribed for only 12.6% of cats at the time of testing (**Table 3**). Although the proportion of cats for which heartworm preventive was prescribed was low in all regions, a significant ( $P = 0.03$ ), moderate correlation (correlation coefficient, 0.7) was identified between these proportions and the regional seroprevalence (**Figure 2**). Heartworm preventive was prescribed least frequently in Canada (2.9% of cats tested) and most frequently in the east north central geodivision (19.2% of cats tested).

## Discussion

Seropositivity for heartworm antigen was identified in cats from 35 states in the present study, and the seroprevalence of heartworm infection was highest in regions where the disease is reportedly most

prevalent in the primary reservoir host, dogs.<sup>12</sup> Overall prevalence was 0.4%, and individual state prevalences varied from 0% to 1.6%. This overall prevalence was similar to the prevalence of 0.5% reported for 2007 in a national survey involving cats.<sup>13</sup>

For cats in the present study, exposure (vs no exposure) to the outdoors increased the risk of seropositivity 3-fold. This was not surprising given that mosquitos are required for transmission. However, indoor containment was not fully protective, and 15% of seropositive cats were reported to live solely indoors. Heartworm infection in indoor cats has been reported previously, including 23% of infected cats in Oklahoma,<sup>14</sup> 19% of infected cats in the South,<sup>15</sup> and 32% of infected cats in a national survey.<sup>16</sup>

The sex of cats (male vs female) in the present study was not a significant risk factor for heartworm seropositivity, but reproductive status was a significant risk factor, with sexually intact males having 2.5 times the odds of castrated males. Male cats have been occasionally reported to be at higher risk of natural heartworm infection<sup>5,15,17,18</sup> than female cats and are more likely to develop mature infections following experimental exposure.<sup>19,20</sup>

Most seropositive cats in the present study had clinical signs of disease at the time of testing. As expected, respiratory signs were most common. However, the increased risk of seropositivity in cats with abscesses or bites wounds or oral disease was unexpected. Also unexpected was the marked increase in the odds of seropositivity for cats with retroviral infections, particularly those with FIV infection. In a previous study<sup>5</sup> involving shelter cats, cats with retroviral infection had no increased risk of heartworm infection. It is possible that the aforementioned health conditions share a common predisposing factor, such as outdoor roaming, rather than a causal relationship with heartworm infection.

Although heartworm preventives are highly effective and are recommended for all cats by the American Heartworm Society<sup>1</sup> and the Companion Animal Parasite Council,<sup>21</sup> prescribing of heartworm preventives at the time of testing in the present study was uncommon (Table 3). Cats living in regions with a higher seroprevalence were more likely to have heartworm preventives prescribed than cats in regions with a lower seroprevalence. It is possible that heartworm preventives were prescribed at a different visit for some cats, leading to an underestimation of the proportion of cats protected against infection.

In a survey of 400 shelters and foster agencies in heartworm-endemic southern states, only 23% reported testing any cats for heartworm infection, and only 31% administered heartworm preventives to at least some of their cats.<sup>22</sup> Reasons given for not testing or providing preventives included cost, lack of options for treating heartworm-infected cats, and the opinion that heartworm infection is not as important in cats as in dogs. In a survey of 357 veterinarians, feline heartworm preventives were stocked by 85% of respondents but recommended by only 61%. Actual

compliance was estimated to be a mere 25%.<sup>23</sup> In a university teaching hospital, 80% of dogs were reportedly receiving a heartworm preventive at the time of examination, compared with only 12% of cats.<sup>22</sup>

Sales patterns of heartworm preventives also support the supposition that cats are much less likely to receive protection against heartworms than dogs. One brand of heartworm preventive in 2014 had sales of \$300 million for the canine-labeled product and only \$5 million for the feline-labeled product.<sup>23</sup> A downward trend in cat visits to veterinarians further undermines the opportunity to protect cats against heartworm infection. In a 2011 survey,<sup>24</sup> owners reported that only 60% of cats had been taken to the veterinarian in the past year, compared with 85% of dogs. Of those taken to the veterinarian, cats had a mean of 1.7 visits/y, compared with 2.3 visits/y for dogs.<sup>24</sup> These findings support the findings of the present study that most cats, even those in areas in which heartworm infection is highly endemic, do not receive heartworm preventives.

In cats, the pathological process of heartworm disease is more complex than in dogs.<sup>1</sup> As in dogs, adult heartworms in cats can cause arteritis, pulmonary inflammation, and thromboembolism. However, in cats, the migration of larvae and arrival of immature adult worms in the pulmonary vasculature during the first 4 months of infection is followed by the death of most of the worms. Even though larval development is commonly aborted before the worms mature, cats can be left with persistent heartworm-associated respiratory disease, involving the development of asthma-like clinical signs caused by pulmonary vascular and parenchymal inflammation. In the study reported here, cats seropositive for heartworm antigen were identified in all regions where heartworm infection is reportedly common in dogs. As expected, respiratory disease was the most common clinical sign in these cats. However, the finding that oral disease, abscesses or bite wounds, and retroviral infection also increased the odds of seropositivity suggested that these conditions should be added to the list of indications for heartworm testing.

In the present study, tests were performed at veterinary clinics and animal shelters in accordance with the instructions provided with the point-of-care ELISA that was used. Antigen-antibody complexes may reduce the sensitivity of heartworm antigen testing in both dogs and cats.<sup>25-27</sup> In a study<sup>26</sup> of 6 cats experimentally infected with heartworms via SC inoculation of third-stage larvae, results of antigen testing were positive for only 1 cat, whereas results of antibody testing were positive for all 6 cats. After serum samples were heated to disrupt antigen-antibody complexes, results of antigen testing were positive for 5 of the 6 cats. In a study<sup>27</sup> of serum or plasma samples from 385 free-roaming and shelter cats, antigen detection increased 5-fold from 1.3% to 6.8% after heat treatment.

In studies<sup>28,29</sup> involving comparison of serologic test results to necropsy findings, antigen test results

were positive for 68% to 86% of cats in which adult worms were identified at necropsy, and antibody test results were positive for 32% to 90% of cats in which adult worms were identified. Together, these findings suggest that serosurveys such as that in the present study likely lead to underestimation of the true prevalence of heartworm infection in cats.

Although cats with mature adult heartworm infections may have positive results of heartworm antigen testing, cats with infections aborted in the early adult stage of worm development do not. They may, however, have positive results of anti-heartworm antibody testing. In a study<sup>15</sup> of 215 cats from the South with respiratory and gastrointestinal signs, 6% were seropositive for heartworm antigen, and 44% were seropositive for antibody against heartworm. In other studies, results of antigen and antibody testing in a national survey were positive in 8% and 12%, respectively, of cats with no clinical signs of infection,<sup>30</sup> and results were positive in 9% and 26%, respectively, of cats with cardiopulmonary abnormalities.<sup>31</sup> In a necropsy study<sup>5</sup> of 630 cats at a Florida shelter, 5% had adult heartworms, 7% had positive results of heartworm antigen testing, and 15% had positive results of anti-heartworm antibody testing. In total, 17% of cats had evidence of heartworm infection. The worm burden in these naturally infected cats was low, with 55% having just a single worm and no cat having > 4 worms. Low worm burden and infections with all-male worms (which, unlike female heartworms, are not detected by existing antigen tests) impede the ability of antigen tests to detect infected cats, resulting in an underestimation of true prevalence.

Extrapolation of the estimated seroprevalence of 0.4% to the estimated 85.8 million cats owned in the United States<sup>32</sup> indicates that > 300,000 cats could have a heartworm infection. However, seroprevalence estimates based on heartworm antigen testing, which identifies only adult heartworms and not pathological aborted larval stages, likely represent the tip of the iceberg in terms of the number of cats with heartworm infection and the resulting clinical damage.<sup>1</sup> Given the difficulty in diagnosing heartworm infection during all clinically relevant developmental stages of the parasite and lack of curative treatment options, veterinarians should prioritize increased compliance with national guidelines to protect cats from heartworm infection.<sup>1</sup>

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## Footnotes

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## From this month's AJVR

### Quality assessment of fluconazole capsules and oral suspensions compounded by pharmacies located in the United States

Carine M. Laporte et al

#### OBJECTIVE

To evaluate pharmaceutical characteristics (strength or concentration, accuracy, and precision), physical properties, and bacterial contamination of fluconazole compounded products.

#### SAMPLE

Fluconazole compounded products (30- and 240-mg capsules; 30- and 100-mg/mL oral suspensions) from 4 US veterinary compounding pharmacies.

#### PROCEDURES

Fluconazole compounded products were ordered 3 times from each of 4 pharmacies at 7- or 10-day intervals. Generic fluconazole products (50- and 200-mg tablets; 10- and 40-mg/mL oral suspensions) served as references. Compounded products were evaluated at the time of receipt; suspensions also were evaluated 3 months later and at beyond-use dates. Evaluations included assessments of strength (concentration), accuracy, precision, physical properties, and bacterial contamination. Acceptable accuracy was defined as within  $\pm 10\%$  of the labeled strength (concentration) and acceptable precision as within  $\pm 10\%$ . Fluconazole was quantified by use of high-performance liquid chromatography.

#### RESULTS

Physical characteristics of compounded products differed among pharmacies. Aerobic bacterial cultures yielded negative results. Capsules (30 and 240 mg) had acceptable accuracy (median, 96.3%; range, 87.3% to 135.2%) and precision (mean  $\pm$  SD,  $7.4 \pm 6.0\%$ ). Suspensions (30 and 100 mg/mL) had poor accuracy (median, 73.8%; range, 53.9% to 95.2%) and precision (mean  $\pm$  SD,  $15.0 \pm 6.9\%$ ). Accuracy and precision were significantly better for capsules than for suspensions.

#### CONCLUSIONS AND CLINICAL RELEVANCE

Fluconazole compounded products, particularly suspensions, differed in pharmaceutical and physical qualities. Studies to evaluate the impact of inconsistent quality on bioavailability or clinical efficacy of compounded fluconazole products are indicated, and each study should include data on the quality of the compounded product evaluated. (*Am J Vet Res* 2017;78:421–432)



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