

# Heartworm infection in cats: 50 cases (1985–1997)

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**Objective**—To characterize risk factors, clinical findings, usefulness of diagnostic tests, and prognosis in cats with naturally occurring heartworm infection (HWI).

**Design**—Retrospective study.

**Animals**—50 cats with *Dirofilaria immitis* infection.

**Procedure**—Medical records, thoracic radiographs, and echocardiograms were reviewed and findings compared with appropriate reference populations.

**Results**—Findings suggested that male cats were not predisposed to HWI, domestic shorthair cats were at increased risk, and indoor housing was only partially protective. Fewer cases of HWI were identified in the final quarter of the year, compared with other periods, and prevalence is not apparently increasing. Signs of respiratory tract disease were most common, followed by vomiting. Infection was diagnosed incidentally in > 25% of cats; conversely, 10% of infected cats died suddenly without other clinical signs. Serologic tests were most useful for diagnosis, followed by radiography and echocardiography. Eosinophilia supported the diagnosis. Overall median survival time was 1.5 years but exceeded 4 years in cats surviving beyond the day of diagnosis.

**Conclusions and Clinical Relevance**—Sex does not appear to be a risk factor for HWI in cats, and indoor housing provides only incomplete protection. Signs of respiratory tract disease (dyspnea and cough) are the strongest indicators of HWI in cats, and some radiographic evidence of infection is detected in most cases. Antibody screening for HWI in cats is efficacious, and antigen testing and echocardiography are most useful for making a definitive antemortem diagnosis. (*J Am Vet Med Assoc* 2000;217:355–358)

Although heartworm disease in cats has gained recognition as an important clinical entity, it is still inadequately understood; most information has been derived from individual case reports, small case series, or experimentally induced infections.<sup>1–6</sup> The purpose of the retrospective study reported here was to characterize risk factors, clinical findings, usefulness of diagnostic tests, and prognosis for heartworm infection (HWI) in cats.

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## Criteria for Selection of Cases

Medical records of cats evaluated from 1985 to 1997 at the North Carolina State University Veterinary Teaching Hospital (NCSU VTH) were retrospectively surveyed for a diagnosis of HWI. A diagnosis of HWI was made if heartworms were found at necropsy or by echocardiographic examination, if heartworm antigen was detected by ELISA, or if microfilariae were detected by the modified Knott test. Reference populations included all cats evaluated at NCSU VTH during the same time period (for analysis of risk associated with sex, hair length, and breed), and results of CBC and urinalyses of 50 age- and sex-matched cats (for evaluation of diagnostic usefulness of eosinophilia and basophilia and determination of prevalence of proteinuria) chosen randomly from case records from the same time period.

## Procedures

Proteinuria, measured by use of reagent test strips, was defined as protein content  $\geq 1^+$  in urine with specific gravity  $\leq 1.020$  and without hematuria or pyuria. Serologic testing was performed by use of various commercial tests during the 10-year period. Antigen tests were generally performed in the NCSU VTH Clinical Pathology Laboratory, although in recent years (since 1990), most ( $n = 20$ ) tests were performed in a commercial laboratory<sup>a</sup> that also performed heartworm antibody ELISA. Prior to 1991, echocardiograms were obtained by a board-certified radiologist or cardiologist, whereas after 1991, all echocardiograms were obtained by a cardiologist. Echocardiograms and thoracic radiographs were reviewed by 2 of the investigators (CEA, TCD).

Survival analysis was first performed on all cats and then performed after exclusion of cats that were dead on arrival or died on the day of diagnosis. Survival information and cause of death were derived from medical records and telephone interviews with pet owners and referring veterinarians. Cats that survived for  $\geq 1,000$  days (2.74 years) were considered to have survived HWI on the basis of the presumed longevity of adult *Dirofilaria immitis* in cats.<sup>7</sup>

Statistical analyses included  $\chi^2$  or Fisher exact tests for comparison with reference populations and comparisons of seasonal incidence by yearly quarter (first quarter, Jan to Mar; second quarter, Apr to Jun; third quarter, Jul to Sep; fourth quarter, Oct to Dec). Survival was analyzed by use of Wilcoxon and log-rank tests of survival, and Kaplan-Meier survival curves were constructed. Significance was set at  $P < 0.05$ .

## Results

Twenty-eight (56%) male and 22 (44%) female cats met the criteria for HWI. Mean  $\pm$  SD age was  $6.35 \pm 4.4$

years, and median age was 5 years (range, 1 to 19 years). Evidence of male overrepresentation was not detected by comparison with the hospital reference population of 8,400 cats, of which 4,474 (57%) were male. Forty-two (84%) cats with HWI were domestic cats, of which 31 (74%) were domestic shorthair and 11 (26%) were domestic longhair. Domestic shorthair cats were significantly overrepresented, compared with the control population (41%). The proportion of heartworm-infected cats of exotic breeds (0.5%) was similar to the proportion of cats of exotic breeds in the reference population (0.6%). Housing status (indoor vs outdoor) was known for 48 cats; 13 (27%) cats were housed indoors exclusively, 33 (69%) were housed indoors and outdoors, and 2 (4%) were housed outdoors exclusively.

The diagnosis of HWI was made significantly less often in the 4th quarter of the year (6 cases), compared with the first (13), second (14), or third (17) quarters. Prevalence of HWI did not appear to increase during the study period (Fig 1).

Clinical signs detected at referral were most commonly related to the respiratory tract (32 [64%] cats), with dyspnea (24 [48%]) and cough (19 [38%]) most often noticed. Vomiting was reported by owners in 17 (34%) cats and had been noticed frequently in 8 (16%) cats. Five (10%) heartworm-infected cats were reported to have had vomiting without concurrent signs of respiratory tract disease; vomiting was evident at the time of referral in 7 (14%) cats. Neurologic signs were reported in 7 (14%) cats and included collapse or syncope in 5 (10%) cats. Five (10%) of the cats were dead when submitted to the hospital. Heart murmurs were seldom detected in cats that did not have preexistent heart disease; heart failure was detected in 1 cat with concurrent hypertrophic cardiomyopathy. Heartworm infection was considered to be an incidental finding (not associated with clinical signs) in 14 (28%) of the cats in the study reported here.

Microfilaria were detected in 1 of 8 cats tested. Heartworm antigen was detected by ELISA in 37 (86%) of 43 cats, and antibodies against *D immitis* were detected by ELISA in 19 of 22 (86%) cats. Of the 3 (14%) infected cats that did not have antibodies against *D immitis*, 1 cat had positive results for heart-

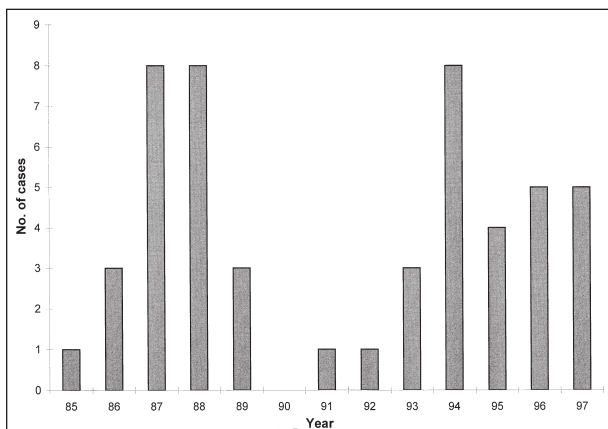


Figure 1—Yearly distribution of 50 cases of heartworm infection in cats during the period from 1985 to 1997. Notice that disease prevalence did not increase substantially during this period.

worm antigen ELISA, 1 cat had evidence of infection detected by echocardiography, and 1 cat had positive results for both of these tests.

Thoracic radiographs were obtained in 41 of the 50 infected cats. Using the criteria for pulmonary artery enlargement established by Schafer et al,<sup>8</sup> 31 (76%) cats had pulmonary artery enlargement. One cat had pleural effusion but had hypertrophic cardiomyopathy in addition to HWI; hypertrophic cardiomyopathy was assumed to be the cause of pleural effusion. Pulmonary parenchymal abnormalities, with or without hyperinflation, were recognized in 30 (73%) cats; a bronchointerstitial pattern was most common, pure bronchial and pure interstitial infiltrative patterns were less common, and alveolar patterns were uncommon. Lung disease, including hyperinflation, was not detected in 12 (24%) of the cats evaluated. Thoracic radiographs of only 10% of cats lacked any indication of HWI (lung disease, pulmonary arterial enlargement, or hyperinflation).

Echocardiograms were performed on 33 cats, and heartworms were detected in 14 (42%). After 1991, when the index of suspicion for heartworm disease in cats was heightened and after which only cardiologists performed each of the echocardiograms, heartworms were detected in 13 of 20 (65%) cats proven to have heartworm infection. Some of these data have been reported in a larger, multi-institutional study.<sup>9</sup>

Among 42 cats with HWI, eosinophilia ( $\geq 1,500$  cells/ $\mu$ l) or circulating basophils were detected in 18 (43%) and 9 (21%) cats, respectively. Differences from the control population ( $n = 50$ ) were significant for eosinophilia (7/50 [14%]) but not for basophils (13/50 [26%]). When eosinophilia was defined as  $\geq 2,300$  cells/ $\mu$ l, better discrimination from the control population was achieved (18/42 [43%] vs 2/50 [4%];  $P < 0.001$ ).

Urinalyses were performed on 31 of the 50 heartworm-infected cats. Proteinuria was detected in 4 of 13 urine samples that were free of blood or evidence of inflammation. This was not significantly greater than the proportion (1 of 12 urinalyses free of blood or evidence of inflammation) detected in the control population ( $n = 50$ ;  $P = 0.07$ ).

Complete survival data were available for 41 of the 50 cats; 11 were alive, 30 were dead, and 9 were lost to follow-up. Two of the latter 9 cats were lost to follow-up immediately after the date of diagnosis, whereas various degrees of follow-up were possible for the other 7 cats. Of the 30 dead cats, 11 were euthanized (7 during the initial hospitalization) and 5 were dead on arrival at the hospital. Heartworm infection was judged to be the cause of death in 10 of the 30 (33%) dead cats. Twelve (40%) cats were thought to have died of other causes, and cause of death could not be determined with adequate certainty in 8 (27%) cats. It is of interest that 6 of these 8 cats died suddenly, but often the duration from diagnosis to death ( $> 1,000$  days in 4 cats) was too great to incriminate heartworms as the cause of death, or there was a concurrent disease that may have contributed to the cats' deaths. Among the 12 cats that died of causes other than HWI, 7 lived  $\geq 1,000$  days and were, therefore, considered to have

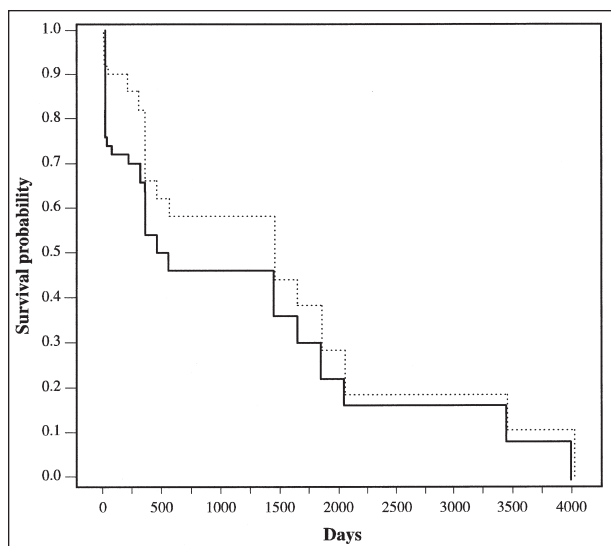


Figure 2—Kaplan-Meier survival estimates for 48 cats with heartworm infection (solid line) and 39 cats with heartworm infection that survived beyond the day of diagnosis of infection (dotted line).

survived HWI. In addition, 2 of the 20 living cats or cats alive when eventually lost to follow-up, lived long enough ( $\geq 1,000$  days) to be classified as survivors. Overall, 9 (18%) were considered to have survived HWI. Twenty-three cats died  $< 1,000$  days after diagnosis. Heartworm infection was judged to be an incidental finding in 14 (28%) of 50 cats.

Median survival (Fig 2) for 39 heartworm-infected cats that survived beyond the day of diagnosis was 1,460 days (mean  $\pm$  SEM,  $1,490 \pm 299$  days; range, 2 to 4,015 days), whereas median survival of all cats ( $n = 48$  with adequate follow-up) was 540 days (mean,  $1,211 \pm 255$ ; range, 0 to 4,015 days). Survival of 11 cats treated with sodium caparsolate (median, 1,460 days; mean,  $1,669 \pm 473$  days) was not significantly different from the 30 cats that did not receive heartworm adulticide treatment (median, 365 days; mean,  $1,107 \pm 329$  days). Likewise, stratification by age ( $\leq 3$  years vs  $> 3$  years), sex, or presence of dyspnea, cough, positive ELISA antigen test results, or detection of adult heartworms by echocardiography did not reveal differences in survival.

## Discussion

Current understanding of HWI in cats has evolved from results of experimental infections, small case series, and individual case reports.<sup>1-6</sup> The study reported here is not large but, to the authors' knowledge, does represent the largest reported case series. Nevertheless, it is accompanied by the inherent weaknesses of any retrospective study.

The age of cats reported here was similar to that of other reports, ranging from 1 to 19 years with a mean age of approximately 6 years.<sup>4</sup> Contrary to reports of clinical cases (without control populations) and experimental studies, male cats did not appear to have higher prevalence of HWI than female cats.<sup>2-4,7,10</sup> This finding is supported by those of recent studies, which indicate that male and female cats are at similar risk for

exposure to HWI<sup>11,12</sup> and development of heartworm disease.<sup>5</sup> Our results (6/50 cases diagnosed during the last quarter of year, 16/50 cases diagnosed during the period from Aug through Dec) differed significantly ( $P = 0.001$ ) from those of Guerrero et al<sup>3</sup> (23/25 cases of HWI in cats in Baton Rouge, La were diagnosed during the period from Aug through Dec).<sup>3</sup> Likewise, our results did not support the growing opinion that the incidence of HWI in cats is increasing.<sup>10,13</sup> We did, however, confirm the logical assumption that a short coat increases the risk of contracting HWI and reconfirm that living indoors is not totally protective.<sup>5</sup>

Reasons for referral or evaluation were similar to those of other studies<sup>2-4</sup> and included dyspnea, cough, vomiting, and, less commonly, syncope, neurologic signs, and sudden death. Importantly, in 28% of cats, we concluded that dirofilariasis was an incidental finding. Neither chylothorax nor pneumothorax, as have been reported in other cats with HWI,<sup>6,14</sup> were observed in the study reported here.

Glomerular disease has been recognized in HWI in dogs<sup>15</sup> and, for that reason, we evaluated results of urinalyses for the cats of the study reported here. With stringent criteria for a diagnosis of proteinuria ( $\geq 1^+$  proteinuria,  $\leq 1.020$  urine specific gravity, and acellular urine) and a small number of urinalyses available, prevalence of proteinuria in cats with HWI (31%) was greater than that of control cats (8%), although differences between groups were not significant.

Diagnostic tests were compared in an attempt to clarify their relative usefulness. These data must be interpreted cautiously, because there is no gold standard, short of necropsy, for the absence of HWI. Therefore, although statements concerning relative sensitivity may be of use, actual sensitivity and specificity of diagnostic tests could not be determined from these data. Serologic tests (ELISA for antigen and antibody) appeared to be most sensitive, detecting 86% of HWI. However, because the antigen test is a gold standard for the diagnosis of HWI, its sensitivity is likely overestimated. Other investigators have shown that the ELISA for heartworm antigen detects  $< 50\%$  of natural infections.<sup>16,17,b</sup> The ELISA for antibody is considered to be quite sensitive (and specific for exposure), but it did not detect 3 of 22 (14%) cats with a diagnosis of HWI in this series; similar but variable (3 to 10%) lack of sensitivity has been confirmed in other recent epidemiologic studies.<sup>12,17,18</sup>

Thoracic radiographs were useful as supportive evidence for heartworm disease in cats; the pulmonary artery enlargement criteria (pulmonary artery  $\geq 1.6 \times$  ninth rib diameter at ninth intercostal space) described by Schafer et al<sup>8</sup> was detected in 31 of 41 (76%) cats. Other findings were as described<sup>8,19,20</sup> and included, in decreasing order, bronchointerstitial infiltrate, bronchial pattern, interstitial infiltrate, and alveolar infiltrate. Pulmonary hyperinflation was also noticed. Thoracic radiographs were entirely lacking in findings suggestive of heartworm disease in 5 (10%) cats.

As described,<sup>5,9,17,20</sup> echocardiography can provide a definitive diagnosis of HWI in cats. Overall sensitivity of 42% for echocardiography for 33 cats in the study report-



ed here was less than that reported by Italian investigators (100%) for a prospective study in a hyperendemic area,<sup>17</sup> less than that of our own prospective clinical study (78%),<sup>5</sup> and less than that of a study of experimentally heavily infected cats (78%).<sup>20</sup> Underscoring the need for an index of suspicion for HWI, sensitivity of echocardiography improved to 65% for cats in our study after 1992 when awareness of HWI in cats was increased, and all studies were performed by a cardiologist.

Routine blood tests were also evaluated, and results confirmed earlier findings that eosinophilia often accompanied HWI in cats<sup>4,10,19</sup>; 43% of cats with HWI in the study reported here had eosinophilia ( $\geq 2,300$  eosinophils/ $\mu$ l). This proportion was significantly greater than that found in the control population (4%). When  $\geq 1,500$  eosinophils/ $\mu$ l was used as the criterion for eosinophilia, differences were still significant, although there was greater overlap between cats with HWI and the control population. The presence of circulating basophils, surprisingly, was not different between groups. Although the number of modified Knott tests performed was small, results confirmed the poor sensitivity of this test (1/8 [13%]).<sup>4</sup>

Although little information concerning the prognosis for HWI in cats is available, it is generally considered to be poor.<sup>2</sup> Indeed, 10% of the cats reported here died suddenly without other signs of HWI, and overall median survival was  $< 2$  years from the date of diagnosis. However, although HWI in cats is life-threatening, our results suggest that at least 18% of the cats with HWI survived the infection (ie, lived  $> 1,000$  days after diagnosis). Furthermore, our data also indicate that median survival is 4 years if cats submitted to the clinic dead or those dying on the day of evaluation are excluded and that in nearly one third of cats, HWI is an incidental finding. Results of the small, retrospective study reported here did not support the use of adulticide in the treatment of HWI in cats, because survival of 11 cats treated with sodium caparsolate was not different from that of 30 cats that did not receive adulticide. Similarly, young age ( $\leq 3$  years), dyspnea, cough, positive results of ELISA for heartworm antigen, detection of adult parasites by echocardiography, and sex did not appear to be associated with survival.

<sup>a</sup>Animal Diagnostics Inc, St Louis, Mo.

<sup>b</sup>McTier TL, Supakorndej N, McCall JW, et al. Evaluation of ELISA-based adult heartworm antigen test kits using well-defined sera from experimentally and naturally infected cats (abstr). *Proc Am Assoc Vet Parasitol* 1993;38:37.

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