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Feline Heartworm Disease: What's Different

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ETIOLOGY AND PATHOPHYSIOLOGY

The domestic cat, though an atypical host, can be parasitized by *Dirofilaria immitis* with resultant heartworm disease (HWD). The clinical manifestations of the disease are different and more severe in this species, but the infection rate is only 5–20% of that of the dog.[1] Experimental infection of the cat is more difficult than in the dog; <25% of L3 reach adulthood. This resistance is also reflected in natural infections, in which feline heartworm burdens are usually less than 10, and typically only 2–4 worms.[2] Other indications of the cat's inherent resistance to this parasite are a shortened period of worm patency, high frequency of amicrofilaremia or low microfilaria counts, and shortened life span of adult heartworms (2–3 years).[2] Nevertheless, studies have shown a prevalence as high as 14% in shelter cats[1] and a study performed at NCSU revealed HWD in 9% of cats presented with cardiorespiratory signs.[3] Furthermore, antibody testing showed 26% of 100 of these cats to have been exposed to HW.[3] Similar to dogs, the male cat is at higher risk for heartworm infection (HWI) than is the female. Aberrant worm migration appears to be a greater problem in cats than in dogs.

The pulmonary arterial response to adult heartworms is more severe than that of the dog, although pulmonary hypertension has infrequently been reported. Dillon demonstrated pulmonary enlargement within one week of transplantation of adults, suggesting an intense host-parasite interaction.[4] A severe myointimal and eosinophilic response produces pulmonary vascular narrowing and tortuosity, thrombosis, and possibly hypertension.[5] Because the feline pulmonary artery tree is smaller than that of the dog and has less collateral circulation, embolization, even with small numbers of worms, produces disastrous results with infarction and even death. Although uncommon, cor pulmonale and right heart failure can be associated with chronic feline HWD and is manifested by pleural effusion (hydro–or chylothorax) and/or ascites. The lung per se also is insulted by HWI, with eosinophilic infiltrates in the lung parenchyma (pneumonitis), pulmonary vasculature, and air spaces. The pulmonary vessels may leak plasma producing pulmonary edema (ARDS?) and type II cells proliferate, both potentially altering O_2 diffusion. The end result is diminished pulmonary function, hypoxemia, dyspnea, and cough.

CLINICAL SIGNS

Cats with HWI may be asymptomatic and, when present, clinical manifestations may be either peracute/acute or chronic.[3,4,6-8] Acute or peracute presentation is usually due to worm embolization or aberrant migration and signs variably include salivation, tachycardia, shock, dyspnea, hemoptysis, vomiting and diarrhea, syncope, dementia, ataxia, circling, head tilt, blindness, seizures, and death. Post-mortem examination often reveals pulmonary infarction with congestion and edema. More commonly, the onset of signs is less acute (chronic form). Reported historical findings in chronic feline HWD include anorexia, weight loss, lethargy, exercise intolerance, signs of right heart failure (pleural effusion; rare), cough, dyspnea, and vomiting. We have found dyspnea and cough to be a relatively consistent findings and, when present, should cause suspicion of HWD in endemic areas.[8]

In an NCSU report of 50 natural cases (Figure 1) of feline heartworm infection, presenting signs were most commonly related to the respiratory system (32 cats; 64%), with dyspnea (24 cats; 48%) being most often noted, followed by cough (19 cats; 38%), and wheezing.[8] Vomiting was reported in 17 (38%) cats and was noted frequently in 8 (16%). Five (10%) heartworm-infected cats were reported to have exhibited vomiting without concurrent respiratory signs and vomiting was a presenting sign in 7 (14%). Neurological signs (including collapse or syncope, which were described in 5 [10%] were reported in 7 (14%) cats. Five (10%) of the cats were dead at the time of presentation. Murmurs were infrequently noted in cats that did not have concurrent heart

disease, independent of heartworm infection. Heart failure was present in 1 cat but this cat had concurrent hypertrophic cardiomyopathy. Heartworm infection was considered to be an incidental finding in 14 (28%) of the cats in this study.

Physical examination is often unrewarding although a murmur, gallop, and/or diminished or adventitial lung sounds may be audible. In addition, cats may be thin and/or dyspneic. If heart failure is present, jugular venous distension, dyspnea, and rarely ascites are detected.

DIAGNOSIS

The diagnosis of HWI/HWD in cats poses a unique and problematic set of issues.[4] First, the clinical signs are often quite different from those of the dog In addition, the overall incidence in cats is low, so suspicion is lessened; eosinophilia is transient or absent; electrocardiographic findings are minimal; and most cats are amicrofilaremic.

Immunodiagnostic methods are also imperfect in cats because of the low worm burdens (1–12, mean = 3) and hence, antigenic load. In a recent study, ELISA antigen tests were positive on sera from 36–93% of 31 cats harboring 1–7 female HW, with sensitivity increasing as female worm burden increased.[9] Cats with male worm(s) were not detected as positive. Therefore, false negative tests occur frequently, depending on test used, maturity and gender of worms, and worm burden. All tests were, however, virtually 100% specific. It is important to realize that infection with signs may be present prior to the presence of detectable antigen (from gravid adult females). McCall reports that, in natural infections, the antigen test detects less than 50% of cases.[10] Snyder and colleagues Levy present differing data from natural infections in which blood was obtained as long as 2 hours post-euthanasia, with the antigen test to be more sensitive than previous reports (74%).[11] Recently an antigen test "for cats" (IDEXX's SNAP^{R} Feline Heartworm Antigent Test) has been marketed. This is an adaptation of the canine test with a reported increase in sensitivity of 15% over conventional antigen tests.

Though less specific, HW antibody tests may be of use in the detection of feline HWI, even when antigen tests are negative. The antibody test may also be useful as a marker for exposure to HWI, even if the cat never develops a mature infection. There are now 2 "in clinic" feline heartworm antibody tests available (HESKA™ SOLO STEP™ FH and Synbiotics' WITNESS^{R} FH).

Thoracic radiographs have been suggested as an excellent screening test in cats. However, Schafer and Barry showed that the most sensitive radiographic criterion (left caudal pulmonary artery greater than 1.6 times the 9th rib at the ninth intercostal space) was only detected 53% of cases.[12] Furthermore, even though most cats with clinical signs have some radiographic abnormality, the findings are not specific to HWD. In addition, a study by Selcer, et al. demonstrated that radiographic findings were often transient and that radiographic abnormalities were found in cats which ultimately resisted maturation of HW and were negative on post-mortem (ie "false positive").[13] Radiographic findings include enlarged caudal pulmonary arteries, often with ill-defined margins, pulmonary parenchymal changes include focal or diffuse infiltrates (interstitial, broncho-interstitial, or even alveolar), perivascular density, and occasionally, atelectasis. Pulmonary hyperinflation may also be evident. Pulmonary angiography has also been utilized to demonstrate radiolucent linear intravascular "foreign bodies," as well as enlarged, tortuous, and blunted pulmonary arteries.

Echocardiography, in our experience, is more sensitive in cats than in dogs.[3,14] Typically, a "double-lined echodensity" is evident in the main pulmonary artery, one of its' branches, the right ventricle, or occasionally at the right atrioventricular junction. We found HW echocardiographically in 78% of 9 cases[3] as did Selcer in 16 experimental infections.[13]

TREATMENT AND PREVENTION

The question arises as to whether HW prophylaxis is warranted for cats because they are not the natural host and because the incidence is low. Necropsy studies of feline HWI in the Southeast have yielded a prevalence of 2.5 to 14% with a median of 7% (Fig 2).[1] When considering the question of institution of prophylaxis, it is worth considering that this prevalence approximates, or even exceeds that of FeLV and FIV infections.[15] A 1998 nationwide antibody survey of over 2000 largely asymptomatic cats revealed an exposure prevalence of nearly 12% (Fig 3).[16] It is also noteworthy that, based on owners' information, nearly one-third of cats diagnosed with HWD at NCSU were housed solely indoors.[8] Lastly, the consequences of feline HWD are potentially dire, with no clear therapeutic solutions. Therefore, I advocate preventative therapy in cats in endemic areas. There are now three drugs with FDA approval and which are marketed for use in cats (Table 1). Ivermectin is provided in a chewable formulation, milbemycin as a flavored tablet and selamectin, a broad-spectrum parasiticide, comes in a topical formulation.

Since the vast majority of cats are amicrofilaremic, microfilaricidal therapy is unnecessary in this species. The use of adulticide is controversial. Thiacetarsemide may be dangerous even in normal cats; Turner and colleagues reported death due to pulmonary edema and respiratory failure in 3 of 14 normal cats given adulticidal doses of thiacetarsemide.[17] Dillon could not confirm this acute pulmonary reaction in 12 normal cats receiving thiacetarsemide, but 1 cat did die after the final injection.[17] More importantly, a significant, though unquantified, percentage of cats with HWI develop pulmonary thromboembolism (PTE) after adulticidal therapy.[4-7] This occurs several days to a week after therapy and may be fatal 20–30% of the time. Because of the risks of adulticidal therapy and because the HW life expectancy is short in cats, recommendations for such treatment are difficult. In 50 cats with HWI, seen at NCSU, 11 received thiacetarsemide. There was no significant difference in survival between those receiving thiacetarsemide and those receiving symptomatic therapy.[8] Because of the lack of clear benefit, this author does not routinely advocate adulticidal therapy in cats. If adulticidal therapy becomes necessary, the dosage is the same as in the dog (2.2 mg/kg over 2 days). Treated cats should be closely confined and observed (preferably in the hospital) for embolic sequelae. Melarsomine cannot be recommended for use in cats.

Cats with HWI should be placed on a monthly preventative and short-term corticosteroid therapy (prednisolone at 1–2 mg/kg q48h–tid) used to manage respiratory signs. For embolic emergencies, oxygen, corticosteroids (dexamethasone at 1 mg/kg IV or IM or prednisolone sodium succinate at 50–100 mg IV/cat) and bronchodilators (theophylline sustained release at 25 mg/kg PO or terbutaline at 0.01 mg/kg SC) may be employed. Bronchodilators have logic, based on the ability of agents, such as theophylline, to improve function of fatigued respiratory muscles. In addition, the finding of hyperinflation of lung fields may indicate bronchoconstriction, a condition for which bronchodilation would be indicated. Nevertheless, this author does not routinely utilize bronchodilators in feline HWD.

The use of aspirin has been questioned as vascular changes associated with HWI consume platelets, increasing their turnover rate and effectually diminishing the antithrombotic effects of aspirin. Conventional doses of aspirin did not prevent angiographically-detected vascular lesions.[19] Dosages of aspirin necessary to produce even limited histological benefit approached the toxic range. Despite this, because therapeutic options are limited; because at conventional doses (80 mg q72h), aspirin is generally harmless, inexpensive, and convenient; and because studies were based on relatively insensitive estimates of platelet function and pulmonary arterial disease, thereby possibly missing subtle benefits, the author continues to advocate aspirin for cats with HWI, but not concurrent with corticosteroid therapy. Management of other signs of HWD in cats is largely symptomatic.

PROGNOSIS

In the aforementioned study of 50 cats with natural heartworm infection, at least 12 cats died of causes other than heartworm disease. Seven of these and 2 living cats were considered to have survived heartworm disease (lived ≥1000 days).[8] The median survival for all heartworm-infected, cats living beyond the day of diagnosis, was 1460 days (4 years; range 2–4015 days), while the median survival of all cats (n=48 with adequate follow-up) was 540 days (1.5 years; range 0–4015 days). Survival of 11 cats treated with sodium caparsolate (mean 1669 days) was not significantly different from that of the 30 managed without adulticide (mean 1107 days). Likewise, youth (≤ 3 years of age), presence of dyspnea, cough, ELISA-positivity for heartworm antigen, presence of echocardiographically-identifiably worms, or gender of the cat did not appear to affect survival.[8]

Figure 1.

Clinical signs (%) in 50 cases of naturally-acquired feline heartworm infection.[8] DYSP = dyspnea, EMESIS = frequent vomition, NEURO = neurological signs, DOA = dead on arrival, INCIDENT = incidental finding.

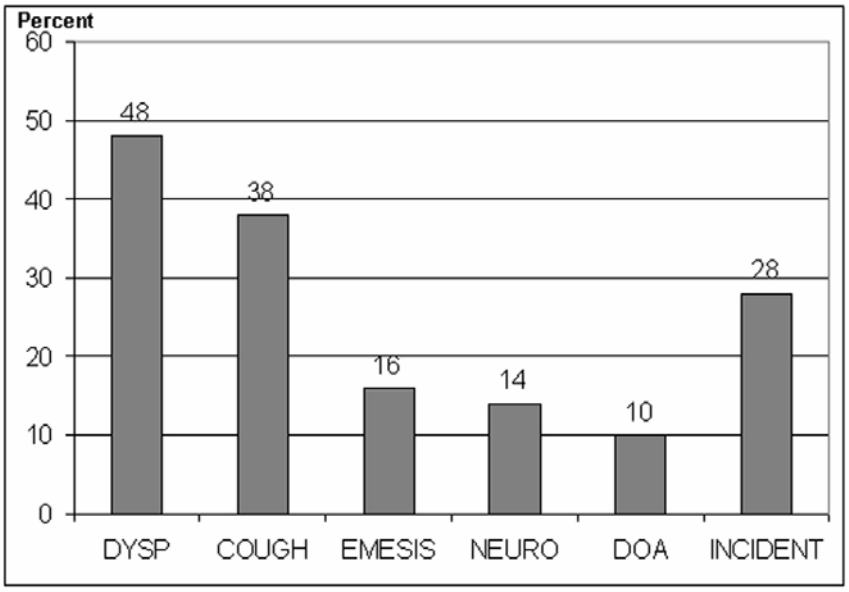

Figure 2.
Necropsy prevalence of heartworm infection in shelter cats.[1] The shaded states are those in which such studies have been completed. One Michigan study, which showed a prevalence of 2%, was an antigen study.

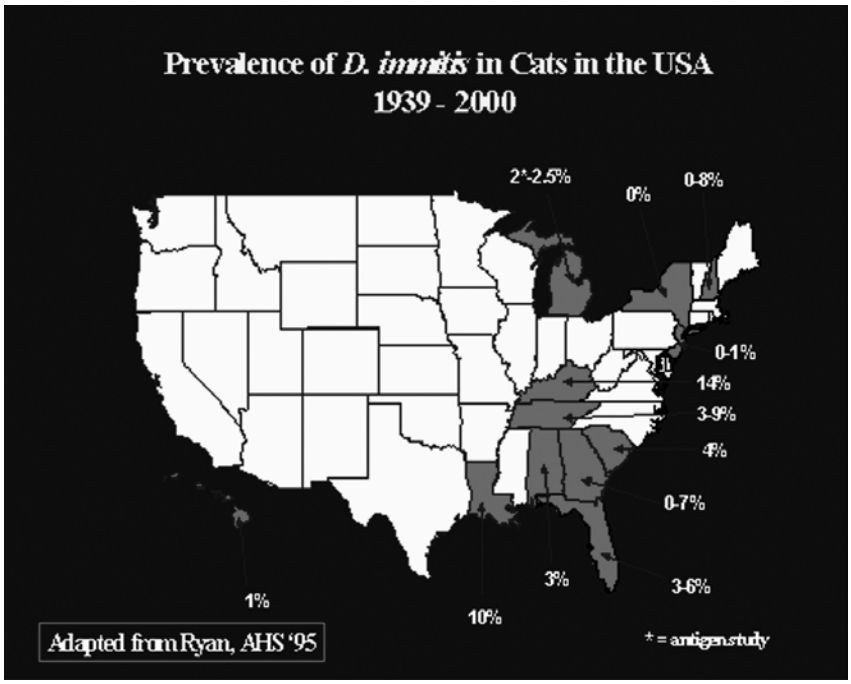

Figure 3.
Prevalence (%) of heartworm exposure in over 2000, largely asymptomatic cats in 19 states (21 regions).[17] NNJ - north New Jersey, CNJ - central New Jersey, LI - Long Island, NY.

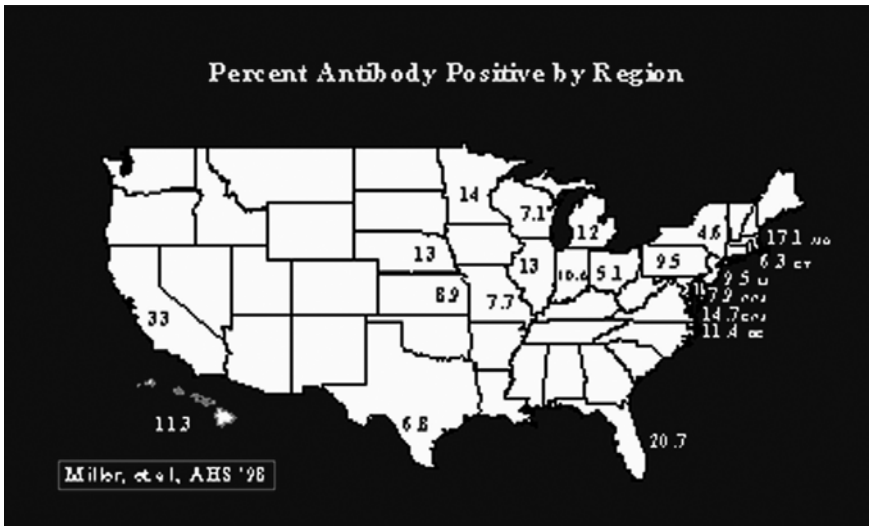

Table 1. Comparisons of macrolides currently in use in cats for heartworm prevention.

Drug	HW	Hook	Whip	Round	Tape	Flea/eggs	Tick	Sarcoptes	Ear Mites
Ivermectin	+	+*							
Milbemycin	+	+		+					
Selamectin	+	+		+		+/+	+	+	+

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