

MAKING THE DIAGNOSIS

Heartworm infection in cats is a more elusive diagnosis than in dogs. Multiple diagnostic tests, some of which may need to be repeated on several occasions, are the most useful methods of clinical confirmation.

HEARTWORM HOTLINE

Feline Heartworm Disease: Separating Fact from Fiction

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The **Heartworm Hotline** column is presented in partnership between *Today's Veterinary Practice* and the **American Heartworm Society** (heartwormsociety.org). The goal of the column is to communicate practical and timely information on prevention, diagnosis, and treatment of heartworm disease, as well as highlight current topics related to heartworm research and findings in veterinary medicine.

Routine wellness visits present the ideal time to discuss the importance of feline heartworm prevention with clients. Although most veterinarians recognize that feline heartworm disease can be serious and even life-threatening, far too few clients invest in heartworm prevention for their cats.

Veterinarians can grow weary of what seems like an uphill battle to convince clients of their cats' need for heartworm prevention. If you've heard one of the following statements from a colleague or client—or even had the same thoughts yourself—chances are you are not alone. Separating the facts about feline heartworm disease from misperceptions is key to educating clients about this often-overlooked disease.

MISPERCEPTION:

“Cats rarely/never get heartworm disease.”

FACT: Although it is true that the prevalence of disease from adult heartworms is less common in cats than in

dogs, it may be more accurate to characterize feline heartworm disease as different from canine heartworm disease, rather than rare.

Unlike dogs, which can harbor large numbers of adult worms, cats are susceptible but imperfect hosts for *Dirofilaria immitis*. Most heartworms in cats die 3 to 4 months after infection, when they are still immature adults—long before infection can produce a positive result on an antigen test.

However, before they die, these immature worms cause disease and damage—a condition known as heartworm-associated respiratory disease, which is characterized by coughing, wheezing, nausea, vomiting, and inappetence. The arrival of these immature worms into the small arteries of the lungs triggers a severe inflammatory response that damages the arteries, bronchioles, and alveoli. Cats are most likely to demonstrate clinical signs of heartworm infection at 2 times: 1) when the immature adult worms reach the pulmonary vasculature and

subsequently die and 2) when the mature adult worms die, usually 2 to 4 years after infection.

MISPERCEPTION:
“I hardly ever see a heartworm-positive cat.”

FACT: The diagnosis of feline heartworm disease is complicated because no single test can consistently detect the various stages of heartworm disease in cats. Often, the combination of serology and imaging results, along with clinical signs, is needed to confirm the diagnosis (**TABLE 1**).



FIGURE 1. Heartworm burdens in cats are much smaller than in dogs; however, infections with just 1 or 2 worms can be life threatening.

Serology

Antigen tests most accurately detect mature female heartworms when they are producing microfilariae. However, not only do cats have more male-only and immature heartworms—neither of which are detectable with antigen tests—their burden of adult heartworms is smaller than that of dogs (**FIGURE 1**). These factors make the detection of heartworms in cats challenging. Even when cats are infected with adult heartworms, these infections are commonly missed by antigen screening.

Antibody tests can detect the presence of infections, both past and present, with male or female worms, as early as 2 months after infection, making them a helpful tool for assessing exposure risk. However, the limitation of antibody testing is that it cannot determine if the cat is currently infected. Because an estimated 10% to 20% of antibody-positive cats are infected with adult heartworms, you should perform antigen testing for these cats at 1- to 2-month intervals. If you suspect adult heartworm infection but the antigen test results are repeatedly “negative,” you may be able to increase test

TABLE 1 Interpretation of Heartworm Diagnostic Procedures and Tests in Cats*

TEST	BRIEF DESCRIPTION	RESULT	INTERPRETATION	LIMITATIONS
Antibody Test	Detects antibodies produced by the cat in response to presence of heartworm larvae. May detect infections as early as 8 weeks after transmission by mosquito	Negative	Lower index of suspicion	Antibodies confirm infection with heartworm larvae, but do not confirm disease causality
		Positive	Increasing index of suspicion; 50% or more cats will have pulmonary arterial disease; confirms cat is at risk	
Antigen Test	Detects antigen produced by the adult female heartworm or from the dying male (>5) or female heartworms	Negative	Lower index of suspicion	Immature or male-only worm infections are rarely detected
		Positive	Confirms presence of heartworms	
Thoracic Radiography	Detects vascular enlargement (inflammation caused by juvenile worms and, later, hypertrophy), pulmonary parenchymal inflammation, and edema (the latter only in acute respiratory distress syndrome [ARDS]-like syndrome)	Normal	Lower index of suspicion	Radiographic signs are subjective and affected by clinical interpretation
		Signs consistent with feline heartworm disease	Enlarged arteries greatly increase index of suspicion	
Echocardiography	Detects echogenic walls of the immature or mature heartworm residing in the lumen of the pulmonary arterial tree, if within the visual window of the ultrasound	No worms seen	No change to index of suspicion	Ultrasonographer experience with heartworm detection appears to influence accuracy rate
		Worms seen	Confirms presence of heartworms in the structure	

*Source: Current Feline Guidelines for the Prevention, Diagnosis, and Management of Heartworm (*Dirofilaria immitis*) Infection in Cats (heartwormsociety.org).

sensitivity by heat pretreatment of the serum sample. In cases where soluble antigen is bound to endogenous antibodies, forming an insoluble unit in the bloodstream known as an “immune complex,” the antigen is essentially blocked from detection. Heat pretreatment is a process that denatures the proteins within the circulating immune complex so that antibodies precipitate and the antigen is freed, making it available for detection.

Because of the challenges in diagnosing feline heartworm disease—and the potential for cats to experience disease and damage from even immature worms—the possibility of heartworm infection in a coughing, asthmatic cat with “no antigen detected” should not be dismissed.

Radiography and Echocardiography

These 2 modalities can confirm heartworm diagnosis and/or assess the likelihood of infection. Imaging can be helpful when the index of suspicion in a cat is



DOES AN INDOOR CAT NEED HEARTWORM PREVENTION?

It's true that outdoor cats are at greater risk of being bitten by infected mosquitoes than their stay-at-home counterparts. But even though a cat that is kept inside is protected from many threats, no residence is a completely sealed fortress against parasites, including *Dirofilaria immitis*. It's important for clients to recognize that the only way to protect cats from this serious threat is year-round administration of heartworm preventives.

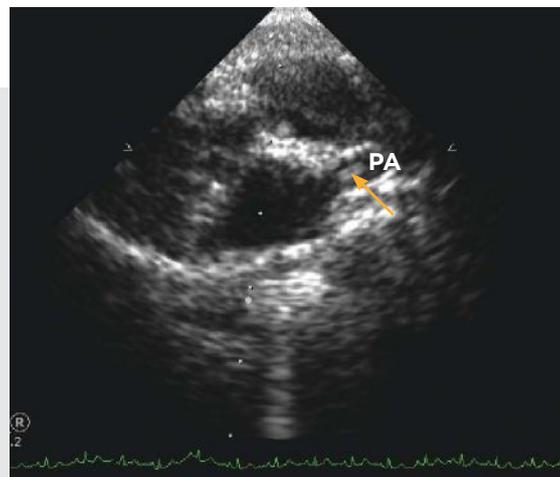


FIGURE 2. Two-dimensional echocardiogram of a cat with heartworm disease. Notice adult heartworms (arrow) within the main pulmonary artery (PA).

elevated on the basis of clinical signs but serology results are inconclusive (**FIGURE 2**).

MISPERCEPTION:

“The risk for heartworms in cats is minimal because most cats live indoors.”

FACT: Outdoor cats are obviously at greater risk of being bitten by infected mosquitoes than are their indoor counterparts, but an indoor lifestyle is no guarantee of safety.

According to a 2014 Vetstreet survey (vetstreet.com/our-pet-experts/do-you-let-your-cat-roam-outside-we-poll-ed-veterinary-professionals-and-readers), roughly three quarters of cat owners house their cats indoors, where they might assume that the risk for heartworm transmission is minimal. However, the Mosquito Control Association (mosquito.org/page/faq) notes that mosquitoes are adept at coming indoors through screens, open doors, attic soffits, and bathroom exhaust vents and often congregate in garages and near doors, seeking indoor entry. Meanwhile, many “indoor” cats may be allowed outdoors on a protected patio or may occasionally slip outside despite their owner’s intentions.

An indoor life can help protect cats from many threats, but it is no panacea when it comes to heartworm prevention. The only way to protect cats from this serious threat is year-round administration of heartworm preventives.

MISPERCEPTION: “I can’t justify the cost of feline heartworm prevention.”

FACT: The adage “an ounce of prevention is worth a pound of cure” applies here.

When clients understand that heartworm infection in cats can only be prevented, not cured, and that just 1 adult heartworm can cause their cat to die suddenly, they can better justify the price of heartworm prevention. Because heartworm preventives for cats cover multiple parasites—some internal only, others internal and external—it makes sense to stress the added value of broad-spectrum protection. Again, indoor cats are not exempt from risk; parasite eggs can be tracked into the house on the soles of shoes or even carried indoors on the coat of a dog that has rolled in infested grass. Pointing out that people can contract intestinal parasites from pets is a compelling message, especially for clients with young children.

CONCLUSIONS

Because cats are susceptible but imperfect hosts for heartworm disease, their worm burdens are much smaller than those of dogs. However, because of cats’ relatively small body size, infections with just 1 or 2 worms can be life-threatening.

Determining the exact prevalence of feline heartworm in your practice area can be difficult, mainly because of testing limitations. A simple approach can be to base your recommendations for heartworm prevention in cats on the comparative risk for heartworm infection in dogs in your area. If canine heartworm disease is endemic to your area, it can be assumed that heartworm prevention for both species is warranted. **TVP**

Elizabeth Clyde-Druin

Elizabeth Clyde-Druin, DVM, received her veterinary degree from the University of Illinois College of Veterinary Medicine in 1991. She is the owner of Clyde’s Animal Clinic in Mattoon, Illinois, and the Animal Family Vet Care Center of Paris in Paris, Illinois. Her special interests are surgery, dentistry, oncology, and internal medicine. She has been on the board of directors of the American Heartworm Society since 2013.



Mirataz™ (mirtazapine transdermal ointment)

For topical application in cats only. Not for oral or ophthalmic use.

CAUTION: Federal law (USA) restricts this drug to use by or on the order of a licensed veterinarian.

Before using this product, please consult the product insert, a summary of which follows:

INDICATION: Mirataz™ is indicated for the management of weight loss in cats.

DOSAGE AND ADMINISTRATION: Administer topically by applying a 1.5-inch ribbon of ointment (approximately 2 mg/cat) on the inner pinna of the cat’s ear once daily for 14 days. Wear disposable gloves when applying Mirataz™. Alternate the daily application of Mirataz™ between the left and right inner pinna of the ears. **See Product Insert for complete dosing and administration information.**

CONTRAINDICATIONS: Mirataz™ is contraindicated in cats with a known hypersensitivity to mirtazapine or to any of the excipients. Mirataz™ should not be given in combination, or within 14 days before or after treatment with a monoamine oxidase inhibitor (MAOI) [e.g. selegiline hydrochloride (L-deprenyl), amitraz], as there may be an increased risk of serotonin syndrome.

HUMAN WARNINGS: Not for human use. Keep out of reach of children. **Wear disposable gloves when handling or applying Mirataz™ to prevent accidental topical exposure.** After application, dispose of used gloves and wash hands with soap and water. After application, care should be taken that people or other animals in the household do not come in contact with the treated cat for 2 hours because mirtazapine can be absorbed transdermally and orally. However, negligible residues are present at the application site and the body of the cat at 2 hours after dosing. In case of accidental skin exposure, wash thoroughly with soap and warm water. In case of accidental eye exposure, flush eyes with water. If skin or eye irritation occurs seek medical attention. In case of accidental ingestion, or if skin or eye irritation occurs, seek medical attention.

PRECAUTIONS: Do not administer orally or to the eye. Use with caution in cats with hepatic disease. Mirtazapine may cause elevated serum liver enzymes (See **Animal Safety** in the product insert). Use with caution in cats with kidney disease. Kidney disease may cause reduced clearance of mirtazapine which may result in higher drug exposure. Upon discontinuation of Mirataz™, it is important to monitor the cat’s food intake. Food intake may lessen after discontinuation of mirtazapine transdermal ointment. If food intake diminishes dramatically (>75%) for several days, or if the cat stops eating for more than 48 hours, reevaluate the cat. Mirataz™ has not been evaluated in cats < 2 kg or less than 6 months of age. The safe use of Mirataz™ has not been evaluated in cats that are intended for breeding, pregnant or lactating cats.

ADVERSE REACTIONS: In a randomized, double-masked, vehicle-controlled field study to assess the effectiveness and safety of mirtazapine for the management of weight loss in cats, 115 cats treated with Mirataz™ and 115 cats treated with vehicle control were evaluated for safety. The vehicle control was an ointment containing the same inert ingredients as Mirataz™ without mirtazapine. The most common adverse reactions included application site reactions, behavioral abnormalities (vocalization and hyperactivity), and vomiting. **See Product Insert for complete Adverse Reaction information.** To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact Kindred Biosciences, Inc. at 888-608-2542. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

EFFECTIVENESS: The effectiveness of Mirataz™ (mirtazapine transdermal ointment) was demonstrated in a randomized, double-masked, vehicle-controlled, multi-site field study involving client-owned cats of various breeds. Enrolled cats were ≥ 1 year of age and had existing documented medical history of ≥ 5% weight loss deemed clinically significant. The most common pre-existing conditions included renal insufficiency, vomiting, and hyperthyroidism. Some cats had more than one pre-existing condition. Cats were randomized to treatment groups in a 1:1 ratio of Mirataz™ to vehicle control. A total of 230 cats were enrolled and received either Mirataz™ (115 cats) or a vehicle control (115 cats) containing the same inert ingredients without mirtazapine. The cats were 2.8-24.6 years of age and weighed 2.1-9.2 kg. The dosage was a 1.5-inch ribbon (approximately 2 mg/cat) mirtazapine or vehicle ointment administered topically to the inner pinna of the cat’s ear. A total of 177 cats were determined to be eligible for the effectiveness analysis; 83 cats were in the Mirataz™ group and 94 cats were in the vehicle control group. The primary effectiveness endpoint was the mean percent change in body weight from Day 1 to the Week 2 Visit. At Week 2, the mean percent increase in body weight from Day 1 was 3.94% in the mirtazapine group and 0.41% in the vehicle control group. The difference between the two groups was significant (p<0.0001) based on a two-sample t-test assuming equal variances. A 95% confidence interval on the mean percent change in body weight for the Mirataz™ group is (2.77, 5.11), demonstrating that the mean percent change is statistically different from and greater than 0.

STORAGE: Store below 25°C (77°F). Multi-use tube. Discard within 30 days of first use.

HOW SUPPLIED: Mirataz™ is supplied in a 5 gram aluminum tube.

MANUFACTURED FOR:
Kindred Biosciences, Inc.
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Burlingame, CA 94010

NADA 141-481, Approved by FDA

Made in USA.

NDC 86078-686-01

REG-MTZBS-008 Rev. 26Apr2018

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