

# Heartworm Management

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The ASV supports the application of the American Heartworm Society guidelines for the prevention, diagnosis, and management of canine and feline heartworms. The ASV also acknowledges that every shelter may not always be able to meet these practices. Resource allocation, capacity for care, compromised welfare brought on by prolonged shelter stays, and risks to population health may warrant alternative approaches to heartworm management.

Regardless of geographic location, sheltering organizations are urged to maintain all dogs, cats, and ferrets on heartworm preventive medications year-round in order to protect individual animal health and welfare and limit disease transmission within the shelter and community. The ASV encourages sheltering organizations to perform screening tests on at-risk dogs. The ASV also encourages all sheltering organizations to institute therapy for infected dogs to reduce pathology and infective potential. If treatment is not an option for dogs in a particular organization, transferring infected dogs to partnering agencies with the capacity to begin treatment is strongly recommended.\*

Organizations choosing to treat infected dogs should ensure that:

- their resources and mission allow for the humane care of exercise-restricted dogs with extended lengths of stay,
- the heartworm management protocol employed minimizes risk of transmission to other animals in the shelter and the community,
- the heartworm management protocol is initiated in a timely manner to limit the potential for further transmission in the shelter and the community,
- resources diverted toward heartworm management do not compromise care of other shelter animals,
- shelter staff, volunteers, and adopters are educated on the importance of adhering to each component of the management protocol, and
- potential adopters are informed of the specific management protocol undertaken and are encouraged to consult with their veterinarian for further guidance.

\*When transporting heartworm-positive dogs, shelters should reference published recommendations for Minimizing Heartworm Transmission in Relocated Dogs.<sup>3</sup>

# References

American Heartworm Society. Current Canine Guidelines for the Prevention,
Diagnosis, and Management of Heartworm Infection in Dogs. Revised 2018.
Available online at: <a href="https://heartwormsociety.org/images/pdf/2018-AHS-Canine-Guidelines.pdf">https://heartwormsociety.org/images/pdf/2018-AHS-Canine-Guidelines.pdf</a>

The mission of the
ASV is to advance and
support the practice
of shelter medicine
in order to improve
community animal
health and well-being.

- 2. American Heartworm Society. Current Feline Guidelines for the Prevention, Diagnosis, and Management of Heartworm Infection in Cats. Revised 2014. Available online at: <a href="https://heartwormsociety.org/images/pdf/2014-AHS-Feline-Guidelines.pdf">https://heartwormsociety.org/images/pdf/2014-AHS-Feline-Guidelines.pdf</a>
- 3. American Heartworm Society and Association of Shelter Veterinarians. Minimizing Heartworm Transmission in Relocated Dogs. Available online at: <a href="https://www.heartwormsociety.org/images/A-News/SKO">https://www.heartwormsociety.org/images/A-News/SKO</a> Transport Guidelines for Web E.pdf

#### Backgrounder: Heartworm Management in Animal Shelters

The management of heartworm disease is a substantial and increasing concern for animal shelters across the United States (<u>Donnett 2018</u>; <u>Fagre 2017</u>; Proctor 2017; <u>Laderman-Jones 2016</u>; <u>AHS-ASV 2014</u>; <u>Polak 2014</u>; <u>Colby 2011</u>). For this reason, the ASV supports thoughtful application and implementation of the American Heartworm Society guidelines for the prevention, diagnosis, and management of canine and feline heartworms (<u>AHS 2018</u>; <u>AHS 2014</u>).

The ASV also acknowledges that shelters may not always be able to meet these practices as issues of resource allocation, capacity for care, compromised welfare brought on by prolonged shelter stays, and risks to population health may warrant alternative approaches to disease management. A "least harms" approach that employs broader treatment options and management practices may be required in many clinical sheltering scenarios in order to protect and improve both individual and community animal health and well-being.

Management approaches that differ from standard recommendations should only be undertaken with a thorough understanding of the risks and benefits to both individual animals as well as the shelter and community animal population and in consultation with a veterinarian. Such approaches should include evaluation of scientific evidence where available as well as direct knowledge of the allocation and restriction of resources faced by each individual sheltering organization.

#### Prevention

Heartworms and their vectors have been found in all 50 states and incidence of infection continues to increase (AHS 2018; Rehm 2017; Bowman 2009). Additionally, the influence of microclimates, biological adaptations of mosquito vectors, and variations in biological characteristics of mosquito vectors ensure year-round risk of transmission regardless of geographic location (AHS 2018). For these reasons, sheltering organizations are urged to maintain all at-risk dogs, cats, and ferrets on heartworm preventive medications year-round in order to protect individual animal health and welfare and limit disease transmission within the shelter and community.

Shelters are encouraged to use FDA-approved heartworm preventive products according to labeled directions whenever possible. However, extra-label use of ivermectin is a common method of heartworm prevention in animal shelters (AHS-ASV 2014; Colby 2011). Such use should only be considered when access to FDA-approved products is not available or feasible. In addition, such preventive protocols should only be employed under the guidance of a veterinarian with direct knowledge of the sheltering program and its animal population. Steps should be taken to minimize risks of toxicity (e.g., dilution of stock product and the use of dosing charts) and with recognition that the dose to be administered varies widely based on intended effect (e.g., heartworm preventive vs. endoparasiticide vs. ectoparasiticide vs. microfilaricide) (Budde 2017).

#### Diagnostic Testing

The ASV encourages sheltering organizations to perform screening tests on at-risk dogs in order to identify those that are infected. In animal shelters, the decision to pursue diagnostic screening tests, including those for heartworm disease, should consider availability and accuracy of testing methodologies, and the impact of testing on shelter operations, animal health, and human health.

Heartworm infection in cats and ferrets is a more difficult diagnosis, often requiring serology and thoracic radiography +/- echocardiography. Because these species do not pose a risk for heartworm transmission, testing is usually reserved for those exhibiting suggestive clinical signs.

In animal shelters, consideration should be given to antigen testing in tandem with microfilaria testing. Although antigen testing is the most sensitive diagnostic method, microfilaria testing can serve as confirmation of a positive antigen test, help identify infected dogs in the presence of antigen blocking, allow for estimation of the microfilarial burden, and identify dogs that serve as reservoirs for further transmission (AHS 2018).

A concentration technique such as the modified Knott test is the most accurate means of microfilaria testing (Box 1); however, microscopic examination of a drop of fresh blood under a coverslip or examination of a blood sample for movement above the buffy coat in a hematocrit tube can aid in identification of microfilaria. Although insensitive when low numbers (50-100/ml) of microfilariae are present, in such patients the potential for severe reaction after microfilaricide administration and the threat of acting as a reservoir of infection are low (AHS 2018). Based on analysis of a Mississippi shelter dog blood bank, blood smear evaluation can be expected to identify 38% of antigen positive samples, whereas modified Knott testing should identify 58% of antigen positive samples (Donnett 2018).

## Management of Infected Dogs

Regardless of the specific disease management protocol undertaken, the ASV encourages sheltering organizations to institute therapy for infected dogs to reduce pathology and infective potential. Alternatives to maintaining unmanaged, infected dogs within the shelter population are strongly recommended. These would ideally include timely transfer to partnering agencies or informed adopters with the capacity to begin treatment; however, humane euthanasia, particularly for dogs that are symptomatic or have additional medical or behavioral concerns, may be appropriate.

In an effort to decrease length of stay, many in-shelter treatment protocols opt to alter the standard pre-melarsomine treatment recommendations. AHS protocol recommends the use of macrocyclic lactones during a two-month pre-adulticidal treatment phase to reduce new infections and eliminate existing susceptible larvae (AHS 2018). Other experts contend that this pre-treatment phase is unnecessary, can result in greater worm mass at the time of adulticidal therapy, and contributes to further damage to the cardiopulmonary system (Bowman 2017).

Similarly, alterations of the recommended dosage (10 mg/kg BID for 30 days) of doxycycline pretreatment are common. There are no studies evaluating the impact of alterations in this dosage or duration of doxycycline therapy on canine heartworm disease treatment. One report of human filariasis treatment found that a 3-week duration of doxycycline therapy reduced microfilarial counts but did not alter adult parasite viability (Turner 2006). Standard recommendations also call for completion of the course of doxycycline prior to melarsomine administration to allow for metabolism of *Wolbachia* organisms, separate the host's immune response to those metabolites from that of the heartworms themselves, and to enhance efficacy of the adulticidal treatment (AHS 2018). However, there are no studies evaluating the impact of timing of administration of doxycycline relative to melarsomine treatment.

Melarsomine dihydrochloride is the only treatment labeled for use as an adulticide and is the safest, most efficacious, and fastest way to ensure clearance of adult heartworms. Other therapeutic combinations may be effective adulticides; however, these all require a substantially prolonged treatment course and their safety has not been evaluated. There is evidence of greater risk of short-term complications of some protocols as compared with melarsomine (Ames 2017). For these reasons, the pros and cons of alternative treatment regimens should be carefully weighed (Table 1).

The American Heartworm Society recommends that all dogs be treated with three doses of melarsomine for the safest and most efficacious adulticidal therapy. This course of treatment, consisting

of one injection followed by two injections given 24 hours apart 1 month later, has been shown to result in the death of 99% of immature adult heartworms (L5) (Zoetis 2017, Merial 2010).

For dogs with asymptomatic, mild, or moderate disease, melarsomine dihydrochloride is also labeled for two treatments given 24 hours apart. Limiting the treatment course to two treatments has been shown to result in the death of approximately 91% of immature adult heartworms (L5) and reduces the length of stay of the animal in the shelter system (Zoetis 2017, Merial 2010).

When definitive adulticidal therapy with melarsomine cannot be provided immediately, heartworm-positive dogs should be started on a 4-week course of doxycycline and a monthly preventive with a macrocyclic lactone until such treatment can be provided. To prevent rebound of *Wolbachia* populations, the course of doxycycline should be repeated every 12 months (McCall 2014). Exercise restriction should be also maintained during this time.

Non-arsenical adulticidal protocols are universally less effective than those incorporating melarsomine, may not eliminate all heartworms even after prolonged treatment courses of up to 30 months, and their success is highly dependent upon the age of the heartworms when treatment is initiated (McCall 2005, McCall 2001). During this lengthy treatment period, existing heartworms will continue to damage the heart, lungs, and pulmonary vasculature. Strict exercise restriction is recommended for the entire time that the animal harbors worms. Because of the prolonged duration of management and the increased risk of adverse medical and behavioral effects, this approach is generally not recommended.

Minimizing length of stay in shelters is the key to ensuring good medical and behavioral health and welfare. When the organization chooses a treatment course efficacy, clinical safety, and duration of treatment must all be considered. Foster care should be considered as alternative housing to improve welfare. Regardless of the course pursued, clear documentation of all treatments provided and recommendations for follow-up after adoption should be provided to each adopter.

## Considerations for Animal Relocation Programs

Minimizing disease transmission, including heartworms, is an essential component of shelter medicine practice. Relocation of heartworm-positive dogs should be reconsidered unless life-saving opportunities and resources will be provided at the destination, are not available in the source community, and such relocation is permissible under applicable law.

Administering doxycycline in combination with a macrocyclic lactone eliminates most circulating microfilariae (McCall 2008), thus breaking the cycle of transmission. Furthermore, after such treatment any remaining microfilariae are unlikely to develop into adult worms even if ingested by a mosquito and transmitted to another canid (McCall 2014). When transporting heartworm-positive and recently treated dogs, shelters should reference the recommendations for Minimizing Heartworm Transmission in Relocated Dogs for further guidance.

## **Adopter Education**

Shelters must ensure that shelter staff, volunteers, and potential adopters are educated on the current heartworm status of the dog, cat, or ferret as well as the importance of adhering to each component of the management protocol.

The Heartworm Disease Resource Task Force, a collaboration between AHS and ASV, has released six downloadable brochures for shelters to provide to adopters based on several common scenarios. Titles include:

- What you need to know about heartworm disease and your newly adopted cat
- Adopting a dog from a shelter that does not test for or treat canine heartworm disease
- Adopting a dog from a shelter that tests but does not treat heartworm disease
- Adopting a dog that has tested positive and been treated for canine heartworm disease
- Are you adopting a dog from another area of the country?
- What does a negative heartworm test mean?

When applicable, these brochures should be included in adoption packets.

Adopters must be informed of the specific disease management protocol undertaken with full disclosure of medical records and encouraged to consult with their veterinarian for further guidance.

## **Summary Statement**

The management of heartworm disease in animal sheltering organizations requires different strategies than those used in private practice or other individually-owned pet scenarios. Existing evidence-based guidelines provide a rational basis on which to develop management goals that protect both individual and community animal health and welfare. Regardless of the specific strategies employed, consideration should be paid to prevention of disease and transmission of infection, establishing a reliable diagnosis in at-risk animals, limiting disease progression in affected animals, and taking steps to ensure that disease treatment is provided in a timely, safe, and effective manner.

#### References

American Heartworm Society. 2018. <u>Current Canine Guidelines for the Prevention, Diagnosis, and Management of Heartworm (Dirofilaria immitis)</u> Infection in Dogs. Available online at: https://www.heartwormsociety.org/images/pdf/2018-AHS-Canine-Guidelines.pdf

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Additional	Resources
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Takin' it to Heart Part 1

Takin' it to Heart Part 2

<u>Frequently Asked Questions on Heartworm Treatment in Shelters</u>

**Adopter Educational Brochures** 

<u>Updates on Heartworm Disease Management for Animal Shelters</u>

**Shelter Heartworm Survey Study** 

# Box 1. Modified Knott Test (AHS 2018)

- 1. Mix 1.0 ml of EDTA blood with 9.0 ml of 2% formalin in a centrifuge tube.
- 2. Invert the tube several times to mix the blood and formalin solution, lysing the red blood cells.
- 3. Place the tube in a centrifuge and spin at 1100-1500 rpm for 5-8 minutes.
- 4. Pour off the liquid.
- 5. Add one drop of methylene blue stain to the sediment.
- 6. Transfer a drop of stained sediment onto a microscope slide and apply a cover slip.
- 7. Examine the slide under low power (10x objective lens) for the presence of microfilariae.

Table 1. Adulticidal Protocol Comparison

Protocol	<u>Description</u>	Adulticidal Efficacy	<u>Treatment</u> <u>Duration</u>	<u>Advantages</u>	<u>Disadvantages</u>	Materials Cost <sup>a</sup>	Cost of Careb	<u>Total</u> <u>Cost<sup>c</sup></u>	References
Split dose melarsomine (3 inj.) + doxycycline	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Days 30 and 31; doxycycline hyclate 10 mg/kg q12h orally x 30 days	No data available.	N/A	Decreased severity of pulmonary pathology and reduced thrombi     Reduced respiratory complications and disease-related deaths     No risk of resistance	•2 months activity restriction	\$145	N/A	N/A	Kramer 2011 Nelson 2017
	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Days 30 and 31; intermittent doxycycline hyclate 10 mg/kg/day <sup>d</sup> ; ivermectin 6 mcg/kg orally weekly	93%	9 mos.	Decreased severity of pulmonary pathology and reduced thrombi     Reduced respiratory complications and disease-related deaths     No risk of resistance     High adulticidal efficacy	•2 months activity restriction •High cost of care (>\$150)	\$269	\$1,350	\$1,619	McCall 2008 Kramer 2011 Nelson 2017
Split-dose melarsomine (3 inj.)	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Days 30 and 31	99%	31 days	No risk of resistance     High adulticidal efficacy	•2 months activity restriction	\$135	\$130	\$265	Zoetis 2017, Merial 2010
	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Days 30 and 31	100%	31 days	No risk of resistance     High adulticidal efficacy	•2 months activity restriction	\$135	\$130	\$265	McCall 2008
Standard dose melarsomine (2 inj.) + doxycycline	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Day 2; doxycycline hyclate 10 mg/kg q12h orally x 30 days	No data available.	N/A	1 month activity restriction     No risk of resistance	Less adulticidal efficacy compared to split-dose protocols	\$100	N/A	N/A	
Standard dose melarsomine (2 inj.)	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Day 2	91%	48 hrs.	1 month activity restriction     No risk of resistance     Low materials costs (<\$100)     High adulticidal efficacy	Decreased efficacy compared to split-dose protocols	\$90	\$10	\$100	Zoetis 2017, Merial 2010
Single dose melarsomine (1 inj.)	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection	52%	Single treatment	No risk of resistance     Low materials costs (<\$100)     Single injection	Poor adulticidal efficacy	\$45	\$5	\$50	Zoetis 2017, Merial 2010
Moxidectin + imidacloprid + doxycycline	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month; doxycycline hyclate 10 mg/kg q12h orally x 30 days	36%	6 mos.	Decreased upfront materials costs	Prolonged activity restriction Poor adulticidal efficacy High cost of care (>\$150)	\$82	\$900	\$982	Bendas 2017
	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month; doxycycline hyclate 10 mg/kg/day x 15 days	62%	11 mos.	Decreased upfront materials costs	Prolonged activity restriction Poor adulticidal efficacy High cost of care (>\$150) Increased coughing during treatment compared to melarsomine protocols	\$137	\$1,650	\$1,787	Ames 2017
	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month; doxycycline hyclate 10 mg/kg q12h orally x 30 days	96%	10 mos.	High adulticidal efficacy	Prolonged activity restriction High cost of care (>\$150)	\$130	\$1,500	\$1,630	Savadelis 2017

	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month; doxycycline hyclate 10 mg/kg q12h orally x 30 days	100%	9 mos.	•High adulticidal efficacy	Prolonged activity restriction High cost of care (>\$150)	\$118	\$1,350	\$1,468	Chandrashekar 2014
Moxidectin + imidacloprid	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month	No data available.	N/A	Decreased upfront materials costs	Prolonged activity restriction	N/A	N/A	N/A	
	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically every 2 weeks	No data available.	N/A	Decreased upfront materials costs	Prolonged activity restriction	N/A	N/A	N/A	
Ivermectin + doxycycline	Ivermectin (6 mcg/kg) orally once per month; doxycycline hyclate 10 mg/kg q 12h x 30 days	No data available.	N/A	Decreased upfront materials costs	Prolonged activity restriction     Potential for increased risk of resistance	N/A	N/A	N/A	Bowman 2012
	Ivermectin (6 mcg/kg) orally q 15 days; doxycycline hyclate 10 mg/kg q 12h x 30 days	73%	10 mos.	•Low materials costs (<\$100)	Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150)	\$60	\$1,500	\$1,560	Grandi 2010 Bowman 2012
	Ivermectin (6 mcg/kg) orally weekly + intermittent doxycycline 10/mg/kg/day <sup>d</sup>	78%	9 mos.	Decreased upfront materials costs	Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150)	\$134	\$1,350	\$1,484	McCall 2008 Bowman 2012
Moxidectin	Moxidectin (0.17 mg/kg) subcutaneous injection every 6 months	No data available.	N/A	•Single injection	Prolonged activity restriction	\$20	N/A	N/A	
Ivermectin	Ivermectin (6 mcg/kg) orally once per week	20%	9 mos.	Decreased upfront materials costs	Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150)	\$180	\$1,350	\$1,530	McCall 2008 Bowman 2012
	Ivermectin (6 mcg/kg) orally once per month	56%	16 mos.	•Low materials costs (<\$100)	Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150)	\$80	\$2,400	\$2,480	McCall 1998 Bowman 2012
Doxycycline	Intermittent doxycycline 10 mg/kg/day <sup>d</sup>	9%	9 mos.	•Low materials costs (<\$100)	Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150)	\$44	\$1,350	\$1,394	McCall 2008 Bowman 2012

a = Cost for treatment of a 20kg dog at the following rates: melarsomine - \$23/ml; doxycycline - \$42/30 days; labeled monthly ivermectin heartworm preventive - \$5/dose; topical moxidectin + imidacloprid - \$12/dose

b = Cost of care estimated at \$5 per day

c = Total cost = Materials cost + Cost of care

d = Intermittent doxycycline protocol = administration during weeks 1-6, 10-11, 16-17, 22-25, 28-33