

# Canine Heartworm Infection

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## P Profile

### Definition

- Disease of the pulmonary vasculature caused by the parasite *Dirofilaria immitis* (Figure 1)

### Geographic Distribution

- *D immitis* is found in all 50 states, with increased prevalence in warmer climates.

### Transmission

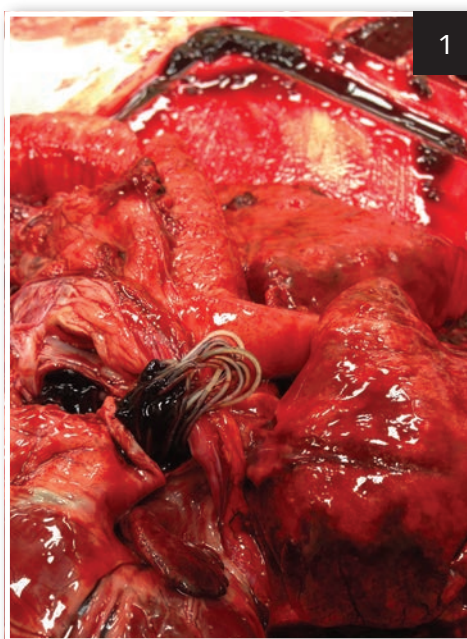
- Mosquitoes extract the L1 microfilarial stage of *D immitis* from an infected dog.
  - L1-L3 molting occurs within the mosquito.
  - The L3 larval stage enters the bloodstream of another dog when the mosquito bites.
  - L3-L5 (adult) molting occurs within the dog.

### Risk Factors

- Any dog that does not receive preventive medication is at risk for heartworm disease.
- In endemic areas, up to 45% of dogs that do not receive preventive medication can be expected to have heartworm disease.<sup>1</sup>

### Pathophysiology

- Adult heartworms lodge in the pulmonary artery and reproduce.
- The direct endothelial contact of adult worms induces an inflammatory response



Gross photo of *Dirofilaria immitis* in the pulmonary artery of a dog.

Courtesy Dr. Julia A. Conway

- (ie, arteritis) that causes endothelial thickening.
  - The degree of host immune response directly influences the extent of the disease process.
- Blood flow obstruction (by the presence of worms) and endothelial thickening can lead to pulmonary hypertension and fibrosis.
- Antigen-antibody complexes can cause microvascular and glomerular damage.
- Embolism of dead worm fragments and fibrin clots can lead to hypoxemia.
- Larger worm burdens can cause caval syndrome.
  - Worms back up into the right ventricle

**Heartworm disease is the most easily preventable cause of canine pulmonary disease.**

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and atrium and become entangled in the tricuspid apparatus.

- ❑ Shear force of RBCs against the worms creates intravascular hemolysis, hemoglobinemia, and hemoglobinuria.
- ❑ Volume overload because of tricuspid and/or pulmonary insufficiency and right ventricular systolic dysfunction can lead to signs of right-sided heart failure.
- ❑ Volume underload of the left side of the heart can cause hypovolemia and shock.

### Clinical Signs

- Many dogs with *D immitis* infection have no signs, but cough, exercise intolerance, and lethargy may be seen.
- Caval syndrome is the most severe form of heartworm disease.
  - ❑ Patients may present with pale mucous membranes, pronounced right-sided heart murmur, shock, hemoglobinuria, hemoglobinemia, and jugular pulsations.
  - ❑ Sudden death may occur.

### Treatment Schedule

- |                          |  |
|--------------------------|--|
| <b>Day 0 (diagnosis)</b> | <ul style="list-style-type: none"> <li>• Execute staging (examination, laboratory studies, thoracic radiography).</li> <li>• Begin doxycycline at 10 mg/kg q12h for 3 weeks.</li> <li>• Begin oral macrocyclic lactone once monthly.</li> <li>• Recommend moderate rest and/or corticosteroid if signs are present.</li> </ul> |
| <b>Day 60</b>            | <ul style="list-style-type: none"> <li>• Administer diphenhydramine at 2.2 mg/kg PO or parenterally.</li> <li>• Administer melarsomine at 2.5 mg/kg via deep lumbar epaxial injection.</li> <li>• Administer NSAID or corticosteroids as indicated.</li> <li>• Enforce strict cage rest.</li> </ul>                            |
| <b>Day 90</b>            | <ul style="list-style-type: none"> <li>• Administer diphenhydramine at 2.2 mg/kg PO or parenterally.</li> <li>• Administer melarsomine at 2.5 mg/kg via deep lumbar epaxial injection twice 24 hours apart.</li> <li>• Administer NSAIDs or corticosteroids as indicated.</li> <li>• Enforce strict cage rest.</li> </ul>      |
| <b>Days 120-150</b>      | <ul style="list-style-type: none"> <li>• Begin gradual return to activity.</li> <li>• Continue monthly macrocyclic lactone.</li> <li>• On day 120, test for microfilariae, and, if positive, retest in 4 weeks</li> </ul>  |
| <b>Day 240</b>           | <ul style="list-style-type: none"> <li>• Perform antigen testing to confirm elimination of adult worms.</li> </ul>   |

## **Dx** Diagnosis

### Laboratory Findings

- Serum chemistry panel is often within reference ranges.
  - ❑ In more severe cases, increased liver enzyme activity may be present because of hepatic congestion from right-sided heart failure.
- Caval syndrome
  - ❑ Azotemia
  - ❑ Hemoglobinemia
  - ❑ Hemoglobinuria
- CBC may show eosinophilia.

### Imaging

#### Radiography

- Enlarged right side of heart (*reverse-D* appearance on VD view)
- Prominent main pulmonary artery bulge
- Blunted, tortuous vessels are noted most often in the caudal lung lobes.
  - ❑ Dorsoventral projection is best for evaluation of pulmonary vasculature.

#### Echocardiography

- In general, abnormal findings will not be noted with uncomplicated heartworm disease.
- Right ventricular dilation or hypertrophy and tricuspid or pulmonic valve insufficiency may be present with more severe disease.
- Worms may be visualized in the pulmonary arteries, but quantification of worm burden is difficult.
- Echocardiography results may provide good confirmation for caval syndrome.
  - ❑ Worms can be visualized in the right atrium/right ventricle.

## Additional Diagnostics

- Antibody testing is not often performed.
- Antigen testing is preferred.
  - Tests for the presence of mature adult female worms; heartworm larvae must have been present 6 months for a positive test result.
  - The test is very sensitive and nearly 100% specific.
- Microfilariae testing is confirmatory, but differentiation from microfilariae of *Acanthocheilonema reconditum* (formerly *Dipetalonema reconditum*) is important.
  - Confirms that the dog is contagious via mosquito vector
  - Negative results may occur if a dog receives macrocyclic lactone preventive medication.
  - Helps predict protocol for possible adverse reaction to treatment

## Tx Treatment

- To determine severity of disease and help predict therapy response and potential posttreatment complications, pretreatment evaluation (ie, staging) should be performed.
  - Thoracic radiography (2 lateral views and 1 DV view)
  - CBC and serum chemistry panel to evaluate for underlying systemic disease and ensure patient is healthy enough for adulticide therapy
  - Urinalysis to evaluate for proteinuria and bilirubinuria
  - Confirmatory heartworm test (eg, microfilariae or repeat antigen testing)
  - Thorough physical examination
  - History, including time patient was without heartworm prevention, prevalence, and severity of clinical signs at home

## Heartworm at a Glance: Cats vs Dogs

### Cats

- 1%–10% of third-stage infective larvae (L3) survive
- Low maturation rate
- Microfilariae uncommon
- Worms survive 2–4 years
- 1–5 worms present
- Smaller adult worms

### Dogs

- 75% of third-stage infective L3 survive
- High maturation rate
- Microfilariae common
- Worms survive 5 years
- Many worms present
- Larger adult worms

## Adulticide Therapy

- Melarsomine dihydrochloride (Immiticide, merial.com) is approved for use by the FDA.
- Treatment with macrocyclic lactone immediately following diagnosis may decrease or eliminate microfilariae and eliminate L3 and early L4 larval stages.<sup>2</sup>
  - These stages are not proven to be eliminated by melarsomine dihydrochloride.

## Adjunct Therapy

- Doxycycline is used to eliminate *Wolbachia pipientis*, a symbiotic bacterium harbored by *D immitis*.<sup>3</sup>
  - Doxycycline is often difficult and/or expensive to obtain; minocycline is a common replacement.
  - This therapy weakens adult worms and makes them less fertile.
  - Doxycycline may improve pulmonary pathology, as *Wolbachia* spp have been shown to contribute to pulmonary inflammation.<sup>3</sup>
- Corticosteroids are often recommended if the dog shows clinical signs (eg, coughing).
- Diphenhydramine can be

administered before melarsomine administration.

## Alternative Therapy

- A *slow-kill* method of placing a dog on macrocyclic lactone and/or doxycycline and waiting for worms to die is not recommended.<sup>1</sup>
  - The potential exists for irreversible heart damage while waiting up to 5 years for all worms to die.
  - Risk for thromboembolism exists until all worms have died and are absorbed.
  - It selects for macrocyclic lactone resistance.

## Client Education

- Strict cage rest throughout the duration of treatment is crucial to prevent life-threatening pulmonary embolism caused by dead worms.
- Gradual return to activity can take place 6–8 weeks after final administration of melarsomine.

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## Rx Medications

### Melarsomine

- 2.5 mg/kg via deep lumbar epaxial IM injection
  - After 1 month, 2 additional injections should be administered 24 hours apart.
- Adverse effects include pain at injection site, lethargy, and allergic reaction.

- If the patient is not receiving corticosteroids, discomfort can be alleviated with NSAIDs for several days following injection.

### Doxycycline

- 10 mg/kg q12h for 3 weeks starting at time of diagnosis
- Minocycline can be used at the same dose if doxycycline is unavailable.

### Macrocyclic Lactone

- Preventive medications can be started at diagnosis and continued for life.

### Prednisolone

- Often used to decrease pulmonary inflammation in patients with clinical signs
- 1–2 mg/kg q12h

### Diphenhydramine

- Often used to help prevent or decrease allergic reactions associated with adulticide therapy
- Should be used before administration of melarsomine therapy
  - 2.2 mg/kg PO or parenterally 1–2 hours before melarsomine injection

## Heartworm Prevention Options for Dogs



### Monthly Oral

#### Ivermectin

- Heartgard (heartgard.com)
- Heartgard Plus (heartgard.com)
- Iverhart Max (virbacvet.com)
- Iverhart Plus (virbacvet.com)
- Pet Trust Plus (pettrust.com)
- Tri-Heart Plus (triheartplus.com)

#### Milbemycin oxime

- Interceptor (interceptor.novartis.us)
- Sentinel (sentinelpet.com)
- Sentinel Spectrum (ah.novartis.com)
- Trifexis (trifexis.com)

### Monthly Topical

#### Selamectin

- Revolution (zoetis.com)

#### Moxidectin

- Advantage Multi (bayerdvm.com)

### 6-Month Injectable

#### Moxidectin

- ProHeart 6 (proheart6.com)



## Follow-up

- All adult heartworms should be eliminated within 1–2 months of final melarsomine injection.
  - Six months after completion of melarsomine therapy, results of antigen testing should be negative.
    - If results are positive, adult infection is most likely still present, and adulticide therapy should be restarted.
    - Testing may also be performed after 6 additional months to determine whether all worms have died.



## In General

### Prognosis

- Prognosis is good to excellent with treatment.
  - If untreated, prognosis is variable.

### Relative Cost

- Depending on size of dog and relative cost for melarsomine therapy and

associated medication: \$\$-\$\$\$

- Heartworm disease staging: \$\$-\$\$\$
- Relative cost for preventive medication, yearly: \$\$

#### Cost Key

\$ = up to \$100  
\$\$ = \$101-\$250  
\$\$\$ = \$251-\$500  
\$\$\$\$ = \$501-\$1000  
\$\$\$\$\$ = more than \$1000

#### Prevention

- Heartworm disease is preventable with administration of macrocyclic lactones (see **Heartworm Prevention Options for Dogs**).
  - Monthly oral
    - Ivermectin
    - Milbemycin oxime
  - Monthly topical
    - Selamectin
    - Moxidectin
  - 6-Month injectable
    - Moxidectin
- Prevention should be started at 8 weeks of age and continued for life.
  - These medications also have efficacy against some internal and external parasites. ■ **cb**

See **Aids & Resources**, back page, for references & suggested reading.

For More



See the companion article, **Feline Heartworm Infection**, on page 69 of the April 2014 issue of *Clinician's Brief* or online at [cliniciansbrief.com/feline-heartworm-infection](http://cliniciansbrief.com/feline-heartworm-infection).

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