Canine Heartworm Infection

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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.¹

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

### 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.

### Treatment Schedule

| Day 0 (diagnosis) | Execute staging (examination, laboratory studies, thoracic radiography).
|                   | Begin doxycycline at 10 mg/kg q12h for 3 weeks.
|                   | Begin oral macrocyclic lactone once monthly.
|                   | Recommend moderate rest and/or corticosteroid if signs are present.
|                   |
| Day 60            | Administer diphenhydramine at 2.2 mg/kg PO or parenterally.
|                   | Administer melarsomine at 2.5 mg/kg via deep lumbar epaxial injection.
|                   | Administer NSAID or corticosteroids as indicated.
|                   | Enforce strict cage rest.
|                   |
| Day 90            | Administer diphenhydramine at 2.2 mg/kg PO or parenterally.
|                   | Administer melarsomine at 2.5 mg/kg via deep lumbar epaxial injection twice 24 hours apart.
|                   | Administer NSAIDs or corticosteroids as indicated.
|                   | Enforce strict cage rest.
|                   |
| Days 120-150      | Begin gradual return to activity.
|                   | Continue monthly macrocyclic lactone.
|                   | On day 120, test for microfilariae, and, if positive, retest in 4 weeks
|                   |
| Day 240           | Perform antigen testing to confirm elimination of adult worms.
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

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.²
  - 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*.³
  - 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.³
- 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.¹
  - 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.

**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

**Note:**

1. Melarsomine dihydrochloride is not approved for use in cats.
2. Doxycycline and minocycline are not approved for use in cats.
3. *Wolbachia* pipientis is not approved for use in cats.
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.

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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.

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

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.

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

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)
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.

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

Cost Key
$ = up to $100
$ = $101–$250
$$ = $251–$500
$$$ = $501–$1000
$$$$ = $1001–$2000
$$$$ = more than $2000

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

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.