Current heartworm issues

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Topics

• Heartworm:
  - risk of infection?
  - testing for heartworm?
  - development of drug resistance?
  - current recommendations for treating heartworm infections
  - surgery on heartworm-positive dogs?

1. A mosquito bites an infected animal, ingesting heartworm microfilariae (pre-L1).
2. Microfilariae mature into heartworm larvae (8-14 days).
3. Larvae enter the dog’s bloodstream, migrate to the heart, lungs, and aorta, and become sexually mature (6-7 months).
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5. Adult heartworms can live within the host and live for >1 years.
**Heartworm in dogs in 2010**

![Map of Canada highlighting heartworm cases](image)

**Heartworm in Canada in 2010**

<table>
<thead>
<tr>
<th>Province</th>
<th># cases</th>
<th>% cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ontario</td>
<td>431</td>
<td>76%</td>
</tr>
<tr>
<td>Manitoba</td>
<td>77</td>
<td>14%</td>
</tr>
<tr>
<td>Québec</td>
<td>41</td>
<td>7%</td>
</tr>
<tr>
<td>British Columbia</td>
<td>8</td>
<td>1.6%</td>
</tr>
<tr>
<td>Alberta/Saskatchewan</td>
<td>4</td>
<td>0.8%</td>
</tr>
<tr>
<td>Nova Scotia/New Brunswick</td>
<td>3</td>
<td>0.6%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>564</strong></td>
<td></td>
</tr>
<tr>
<td>(354 in 2002)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Heartworm in Ontario dogs (2010)**

- How likely is a dog to get infected?
  - 289,229 tested
  - 382 “heartworm positive” (new in 2010)
  - overall “prevalence” = 0.13%
  - ≥ 51% infections acquired in Ontario
  - importation of heartworm: 47 (12%) = “Katrina dogs”
  - 55 (14%) = imports from other states/countries
  - 13 (3%) = travelled outside Canada
  - 83% positive dogs not on heartworm prevention in previous year
Heartworm in Ontario

~80% cases south of highways 402/401/403

How prevalent is disease?

• 46/382 (~12%) heartworm-positive dogs had clinical signs

Heartworm in Canada (2013-2014)

Herrin et al (2017)
Heartworm risk in USA - 2016

Heartworm in Canada

Is the risk of heartworm in Canada changing in dogs/cats?
- What has been the impact of “Katrina” dogs?

Impact of hurricane Katrina dogs?

- Still being imported in to Ontario?
- Tested for heartworm in Louisiana immediately prior to departure for Canada:
  - If test negative, sold as heartworm negative
  - If test positive, often treated with one dose of melarsomine
- Some owners refusing to pay for adulticide treatment
Detection of heartworm infection

- Earliest antigen can be detected = ~5 months
- Earliest microfilariae can be detected = ~6 months
- No justification for testing <7 months of age

Testing for heartworm infection – what has changed?

- Some dogs infected with *D. immitis* are microfilaria positive but test negative for antigen
  ↔ immune complex formation (Little et al 2014)

- Shelter dogs in southeast USA:
  - 7.1% of dogs infected with heartworm:
    - antigen negative / microfilaria positive (Velasquez et al 2014)

American Heartworm Association now recommends annual testing for antigen and microfilariae (AHS 2014)

Testing for heartworm

**Antigen and microfilaria test recommended if:**

- high degree of suspicion of infection
- heartworm prevention history unknown

(AHS 2014)
Testing protocol for new dogs

Before initiating heartworm preventive regimen on dogs ≥7 months old - perform antigen + microfilaria test:

i. immediately
ii. 6 months later
iii. 6 months later
iv. annually thereafter

(AHS 2014)

Is drug resistance developing in heartworm?

- Anecdotal evidence from parts of southern USA (Hampshire, 2005):
  - Increased number of heartworm cases in dogs on heartworm prevention reported to Food and Drug Administration
  - Reason(s)?

- Louisiana dog in Niagara area – heartworm antigen positive + microfilaremic
  - Treated with 3-dose protocol of melarsomine (Immiticide):

<table>
<thead>
<tr>
<th>Days after last melarsomine treatment</th>
<th>Heartworm antigen</th>
<th>Microfilaria concentration in blood</th>
<th>Milbemycin treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>207</td>
<td>Negative</td>
<td>≥ 100/mL</td>
<td>0.74 mg/kg every 2 weeks for 6 weeks</td>
</tr>
<tr>
<td>263</td>
<td>Negative</td>
<td>≥ 100/mL</td>
<td>1.1 mg/kg every 2 weeks for 10 weeks</td>
</tr>
<tr>
<td>340</td>
<td>Negative</td>
<td>6,520/mL</td>
<td>2.0 mg/kg daily for 7 days</td>
</tr>
<tr>
<td>385</td>
<td></td>
<td>355/mL</td>
<td>2.0 mg/kg daily for 8 days</td>
</tr>
<tr>
<td>445</td>
<td>Negative</td>
<td>1,810/mL</td>
<td></td>
</tr>
</tbody>
</table>

(NB Standard microfilaricidal treatment = milbemycin at 0.5 mg/kg)

(Bourguinat et al. 2011)
Resistance of heartworm to preventive drugs?

<table>
<thead>
<tr>
<th>Day</th>
<th>Necropsy + parasite counts</th>
<th>Ivermectin efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16 dogs</td>
<td>20.3-82.9%</td>
</tr>
</tbody>
</table>

Conclusions: The two *Dirofilaria immitis* isolates are resistant to ivermectin. 
"Also resistant to selamectin, milbemycin and moxidectin" (Kaminsky et al 2013)

Implications of drug resistance in heartworm?

- Note: most cases currently (2013) in Mississippi River Valley.
- Avoid moving heartworm-infected dogs out of areas with reports of resistance.
- Confirm that adulticide treatment protocol eliminates both adult parasites and microfilariae.
- Avoid selective pressure against microfilariae, such as underdosing or slow-kill treatments.

Managing dogs infected with *Dirofilaria immitis*
Treating dogs infected with *Dirofilaria immitis*

**Originally:**
- Two treatments with melarsomine at 2.5 mg/kg, IM, 24 hours apart.

Treating dogs with melarsomine

- Two injection protocol (days 1,2) kills ~90% adult parasites.
- Three injection protocol (days 1,30,31) kills ~98% adult parasites.
- Percentage of dogs cleared of infection = less than these figures.

(Keister et al 1992; Vezzoni et al 1992)

Susceptibility of *D. immitis* to macrocyclic lactones and melarsomine

- [Graph depicting parasite development and susceptibility gap between macrocyclic lactones and melarsomine]
**Dirofilaria immitis and Wolbachia**

- Most *D. immitis* infected with *Wolbachia* (intracellular bacteria)

**Treatment with doxycycline at 10 mg/kg BID for 4 weeks:**

- reduces bacteria numbers in all parasite stages for ~12 months.
- reduces pulmonary pathology after melarsomine treatment.

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**Dirofilaria immitis and Wolbachia**

**Treatment with doxycycline at 10 mg/kg BID for 4 weeks:**

- Helps eliminate all developing larvae during first 60 days of infection (McCall et al 2011).
- Gradually suppresses microfilariaemia if given to heartworm-positive dogs (Bazzocchi et al 2008; McCall et al 2008).
- Reduces parasite transmissibility in mosquito after ingestion of microfilariae (McCall et al 2008).

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**Treating dogs infected with *Dirofilaria immitis***

**Now:** 3-dose protocol used for all infections except caval syndrome:

- On days 1, 30 and 31 treat with melarsomine at 2.5 mg/kg, IM
  - safer and more efficacious

**Also:**

(i) Pre-treat with heartworm preventive on days -60, -30 and 1 (if applicable).
(ii) Pre-treat with doxycycline for 4 weeks.
(iii) On days 1 & 30: prednisone at 0.5 mg/kg BID 1st week, 0.5 mg/kg SID 2nd week, 0.5 mg/kg EOD 3rd & 4th week.

**To evaluate efficacy of treatment:**

- At 6 months post melarsomine treatment perform an antigen and microfilaria test.
If melarsomine treatment not possible or contraindicated

- Maintain continuously on macrocyclic lactone (ML) heartworm preventive (i.e. monthly treatment).
- Give doxycycline at 10 mg/kg BID for 4 weeks (can use 5 mg/kg BID?).
- Antigen and microfilaria test every 6 months – continue ML treatment until two negative antigen tests.
- If dog antigen positive after one year, repeat doxycycline treatment.
- Restrict exercise throughout treatment protocol.

Surgery on heartworm-positive dogs?

- No evidence of an increase in perioperative complications in heartworm-positive dogs with no-to-mild clinical signs of heartworm disease (Peterson et al 2014).

(AHS 2014)

For full details see: https://www.heartwormsociety.org/veterinary-resources/american-heartworm-society-guidelines