Outline

• Heartworm disease overview
  – Epidemiology, life cycle, practice guidelines

• Current practices
  – Results from an AHS-ASV survey

• Practical management strategies for shelters
  – Prevention, diagnosis, treatment

Canine Heartworm Disease

I’m a first time dog owner. I recently adopted a dog...and was told he was healthy... The dog was never tested for heartworm... So, my poor boy has heartworm... I don’t understand why they are giving out a lot of potentially sick dogs when they could test them and let the adopting party know what kind of experience and vet bills they will have. I’m so frustrated with the rescue group.
Learning Outcomes

• Recall characteristics pertinent to clinical management of canine heartworm disease

• Understand current practices and challenges to standard guidelines in the shelter setting

• Design management protocols feasible in the shelter setting in light of their risks and benefits

Canine Heartworm Disease

• Prevalence of positive test results
  – Private practice
  
<table>
<thead>
<tr>
<th>Region</th>
<th>Mean Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northeast</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Midwest</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Southeast</td>
<td>4%</td>
</tr>
<tr>
<td>West</td>
<td>1%</td>
</tr>
<tr>
<td>Overall</td>
<td>1%</td>
</tr>
</tbody>
</table>

  – Animal shelters
    • 15% shelter dogs in Florida

• Heartworms are endemic in the U.S.
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Canine Heartworm Disease

- Heartworms are endemic in the U.S.
  - Transport of positive dogs
  - Expansion of wild canid territory
  - Environmental changes
    - New water sources
    - Urban “heat islands”

Canine Heartworm Disease

- Other factors
  - Some mosquito species survive over winter
  - Live and breed for 1-5 months

Risk of transmission is always present!

Canine Heartworm Disease

- L3
- L2
- Microfilaria
Canine Heartworm Disease

- **L4**: 2 to 3 months
  - Immature
  - Adult
- **Mature Adult**: 3 to 4 months

---

<table>
<thead>
<tr>
<th>Who?</th>
<th>Where?</th>
<th>When?</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1 → L2 → L3</td>
<td>Mosquito</td>
<td>10-14 days</td>
</tr>
<tr>
<td>L3</td>
<td>Soft tissue</td>
<td>3-12 days</td>
</tr>
<tr>
<td>L4</td>
<td></td>
<td>2-3 months</td>
</tr>
<tr>
<td>Immature adult</td>
<td>Heart &amp; lungs</td>
<td>3-4 months</td>
</tr>
<tr>
<td>Mature adult</td>
<td></td>
<td>3-7 years</td>
</tr>
</tbody>
</table>

- Remember...
  - We can only test for microfilaria & mature adults
  - Treatment options & protocols vary by life stage

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- Prevention
- Diagnosis
- Treatment
Canine Heartworm Disease

• Prevention
  – Monthly oral or topical preventive OR
  – Bi-annual injectable preventive

• Diagnosis
  – Annual antigen testing
    • Testing prior to changing preventives
    • Following lapse in preventive
    • Tandem mf testing
  – X-rays, echocardiography as indicated

Canine Heartworm Disease

• Treatment
  – Days 0-59
    • Exercise restriction
    • 4-week course of steroids if symptomatic
    • Monthly preventive
    • 4-week course of doxycycline
  – Days 60-91
    • Adulticidal treatment with melarsomine (Days 60, 90, 91)
    • 4-week course of steroids
    • Limit activity to cage rest & leash walks
  – Continued exercise restriction for 6-8 weeks

Current Practices & Challenges

• AHS-ASV working group
  – Identify current practices and needs of shelter veterinarians
  – Create practical guidelines and resources

• February 2014
  – Online survey administered to ASV membership
  – 105 responses
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Current Practices & Challenges

Shelter Type

<table>
<thead>
<tr>
<th>% Shelters</th>
<th>Municipal AC</th>
<th>Private HS/PCA</th>
<th>Sanctuary</th>
<th>Foster Network</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>10</td>
<td></td>
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<tr>
<td>20</td>
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<tr>
<td>30</td>
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<tr>
<td>40</td>
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<td>50</td>
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<tr>
<td>60</td>
<td></td>
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</tr>
<tr>
<td>70</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model</th>
<th>Response %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open Admission</td>
<td>61%</td>
</tr>
<tr>
<td>Limited Admission</td>
<td>36%</td>
</tr>
<tr>
<td>Adoption Guarantee</td>
<td>25%</td>
</tr>
<tr>
<td>Other</td>
<td>10%</td>
</tr>
</tbody>
</table>

Current Practices & Challenges

Annual Canine Intake

- Max: 16,000
- Min: 10
- Average: 4,000

Current Practices & Challenges

Shelter HW Prevalence

- Max: 70%
- Min: 1%
- Average: 9%
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Current Practices & Challenges

- Prevention
  - 66% of shelters provide monthly heartworm preventive
  - 65% shelters use oral ivermectin products on-label

- Other
  - Injectable IVM
  - Whatever is donated

Diagnostic practices

Are dogs tested for heartworm infection?

- Yes, 42.2%
- Some, 48%
- No, 9.8%
How Animal Shelters Can Treat and Prevent Heartworm in Dogs

Current Practices & Challenges

- Diagnostic practices
  - Which dogs are tested?
    - Adoption candidates
    - Those from endemic areas
    - Specific health concerns

Current Practices & Challenges

- When does testing occur?

Current Practices & Challenges

- What type of screening test is used?
Current Practices & Challenges

• Diagnostic practices
  – 48% shelters do additional testing after a positive screening test
    • Repeat screening test
    • Bloodwork
    • Chest x-rays
    • Urinalysis
    • Echocardiogram

• Treatment
  – 85% of shelters treated at least some infected dogs
  – Dogs not treated are
    • Euthanized
    • Placed for adoption without treatment
    • Transferred elsewhere for treatment

Current Practices & Challenges

• Treatment
  What is the adulticide treatment protocol?

<table>
<thead>
<tr>
<th>Percent of Shelters</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>80</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

Which adjunctive treatments are utilized?

<table>
<thead>
<tr>
<th>Percent of Shelters</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>80</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

Current Practices & Challenges
Current Practices & Challenges

- Notable deviations from standard guidelines
  - Prevention
    - Ivermectin is frequently used extra-label for prevention
  - Diagnosis
    - Many shelters do not test dogs for infection
    - A single screening test is frequently used for diagnosis
  - Treatment
    - 2-dose melarsomine treatment protocol is frequently used
    - Adjunctive treatments are inconsistent

Designing Practical Protocols

- Why administer preventives?
  - Infected dogs serve as reservoirs
  - Assistance with other parasites

- Shelter concerns
  - Ivermectin is frequently used extra-label for heartworm prevention
How Animal Shelters Can Treat and Prevent Heartworm in Dogs

Designing Practical Protocols

• Extra-label use of ivermectin

Cost Toxicity

• Understand the Concerns
  – Gene mutation results in inability to move avermectins out of the brain
    • Includes ivermectin, milbemycin, moxidectin, selamectin
  – Toxic dose 4x higher than heartworm preventive dose
  – Treatment
    • Prevent further absorption
    • Supportive care
    • Time (days to weeks)

• Mitigate the Risk
  – Ensure accurate body weight measurements
  – Dilute solution for more accurate dosing
  – Create dosing chart to minimize human error
  – Mutation most common in Collies, Australian Shepherds, Longhaired Whippets, Shetland Sheepdog
    • Selectively avoid use in at-risk breeds
How Animal Shelters Can Treat and Prevent Heartworm in Dogs

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Designing Practical Protocols

• Why obtain a diagnosis?
  – Infected dogs serve as reservoirs
  – Infected dogs have specific medical needs
  – Identify infections sooner, prevent disease progression

• Shelter concerns
  • Many shelters do not test dogs for infection
    • I'm not going to treat – why should I test?
  • A single screening test is frequently utilized for diagnosis

Designing Practical Protocols

• Inadequate diagnostic protocols
  – Many shelters do not perform screening tests

<table>
<thead>
<tr>
<th>Cost</th>
<th>Time</th>
<th>Technical skill</th>
<th>Burdens adopters</th>
<th>Sets poor example</th>
<th>Promotes stigma of shelter adoptions</th>
</tr>
</thead>
</table>

Designing Practical Protocols

• Understand the Evidence
  – Heartworm disease is endemic in the U.S.
  – Mild illness can become life-threatening
  – Mosquito infection rates in kennels with positive dogs were 10x higher than in the community
    • Ignoring disease status facilitates spread
    • Treatment impact greatest where prevalence is low
Designing Practical Protocols

- Mitigate the Risk
  - Time and cost can be minimal

<table>
<thead>
<tr>
<th>Test</th>
<th>Detects</th>
<th>Est. Test Time</th>
<th>Cost</th>
<th>Sample Size</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Microscopy</td>
<td>Microfilaria</td>
<td>5 min.</td>
<td>$</td>
<td>100 uL</td>
<td>80.9%</td>
<td>100%</td>
</tr>
<tr>
<td>Centrifugation Microscopy</td>
<td>Microfilaria</td>
<td>10 min.</td>
<td>$</td>
<td>50 uL</td>
<td>65.5%</td>
<td>100%</td>
</tr>
<tr>
<td>Filtration Testing</td>
<td>Microfilaria</td>
<td>10 min.</td>
<td>$$</td>
<td>1 ml</td>
<td>72.7%</td>
<td>87.7%</td>
</tr>
<tr>
<td>Modified Knott’s Test</td>
<td>Microfilaria</td>
<td>10 min.</td>
<td>$</td>
<td>1 ml</td>
<td>81.8%</td>
<td>100%</td>
</tr>
<tr>
<td>ELISAs</td>
<td>Antigen</td>
<td>5-15 min.</td>
<td>$$</td>
<td>300 uL</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Lateral Flow Tests</td>
<td>Antigen</td>
<td>5-10 min.</td>
<td>$$$</td>
<td>300 uL</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

$ = <$1 per test; $$ = <$5 per test; $$$ = <$10 per test

* Highest reported values are presented.

- Mitigate the Risk
  - Selectively test dogs at high risk
    - Stray
    - Transported from high risk regions
  - Test dogs selected for adoption/transfer
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Designing Practical Protocols

• Inadequate diagnostic protocols
  – Antigen testing

<table>
<thead>
<tr>
<th>High sensitivity</th>
<th>Costly False negatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulk testing</td>
<td></td>
</tr>
</tbody>
</table>

• Inadequate diagnostic protocols
  – Microfilarial testing

<table>
<thead>
<tr>
<th>Inexpensive</th>
<th>Lower sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can direct treatment plan</td>
<td>Technical skill and equipment</td>
</tr>
<tr>
<td>Validates serologic results</td>
<td></td>
</tr>
<tr>
<td>Identify potential for resistance</td>
<td></td>
</tr>
<tr>
<td>No Ag-Ab complex interference</td>
<td></td>
</tr>
<tr>
<td>Lower sensitivity</td>
<td></td>
</tr>
</tbody>
</table>

• Understand the Evidence
  – False negative results can occur
    • Antigen
      – Male only infections
      – Low worm burdens
      – Poor technique
      – Ag-Ab complex interference
      – 7% of negative serum samples were positive after heat treatment
    • Microfilaria
      – Single sex infections
      – Immature life stages
      – On preventive
How Animal Shelters Can Treat and Prevent Heartworm in Dogs

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Designing Practical Protocols

• Understand the Evidence
  – Antigen tests and microfilarial tests provide different information
  – Results may impact management protocols
    • Adverse reactions to circulating mf more likely
      – With milbemycin treatment
        – Dogs <16kg
        – >10,000 mf/ml of blood

Designing Practical Protocols

• Mitigate the Risk
  – Test for microfilaria prior to antigen testing
    • In areas of high prevalence
    • When high counts will alter treatment
  – Test for antigen prior to microfilaria
    • When there is a history of preventive administration
    • Vaccinated, surrendered dogs
  – Heat treatment?
    • Boiling water bath for 10 minutes

Designing Practical Protocols

• Why offer treatment?
  – Heartworm disease is deadly but curable
  – Severely affected dogs may have compromised welfare
  – Most adopters do not want a project, they want a pet

• Shelter concerns
  • 2-dose melarsomine treatment
  • Alternative treatments
Designing Practical Protocols

• Sub-optimal treatment protocols
  - Cheaper than 3-dose protocol
  - Less effective than 3-dose protocol
  - Decreased length of stay
  - Increased risk of complications

Designing Practical Protocols

• Understand the Evidence
  - Laboratory studies
    - 1-dose = 52% adulticidal
    - 2-dose = 90% adulticidal
    - 3-dose = 98-99% adulticidal
  - Field studies
    - Mild infection
      - 2-dose protocol; 90-98% of dogs negative at 4 months
    - Severe infection
      - 3-dose protocol; 89-100% of dogs negative at 4 months

Designing Practical Protocols

• Understand the Evidence
  - Literature review of field and laboratory studies
    - 2 or 3-dose melarsomine treatment protocol
    - Efficacy confirmed by antigen test or necropsy
  - Weighted average efficacy
    - 2-dose protocol = 88%
    - 3-dose protocol = 89%
  - Conclusion
    - 10% of dogs diagnosed and treated for heartworms will have ≥1 heartworm remaining after treatment with either 2-dose or 3-dose protocol
Designing Practical Protocols

• Understand the Evidence
  – “Slow kill” (i.e., use of a preventive alone to kill adults)
    • Monthly oral ivermectin

<table>
<thead>
<tr>
<th>Age of Heartworms At Initiation (Mos.)</th>
<th>No. of Treatments</th>
<th>Efficacy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>14</td>
<td>97.8</td>
</tr>
<tr>
<td>4.5</td>
<td>12</td>
<td>86.2</td>
</tr>
<tr>
<td>5</td>
<td>31</td>
<td>98.7</td>
</tr>
<tr>
<td>5.5</td>
<td>12</td>
<td>52.2</td>
</tr>
<tr>
<td>7</td>
<td>29</td>
<td>94.9</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>56.3</td>
</tr>
</tbody>
</table>

Designing Practical Protocols

• Understand the Evidence - Alternative protocols

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% Efficacy at 36 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent doxycycline</td>
<td>9</td>
</tr>
<tr>
<td>Weekly ivermectin</td>
<td>20</td>
</tr>
<tr>
<td>Weekly ivermectin + intermittent doxycycline</td>
<td>78</td>
</tr>
<tr>
<td>Weekly ivermectin + intermittent doxycycline +</td>
<td>93</td>
</tr>
<tr>
<td>3-dose melarsomine</td>
<td></td>
</tr>
<tr>
<td>3-dose melarsomine</td>
<td>100</td>
</tr>
</tbody>
</table>

Designing Practical Protocols

• Understand the Evidence – Alternative Protocols
  – Doxycycline (30d) + ivermectin (6 mos.)
    • Day 90
      – Negative for mf
    • Day 300
      – 84% improvement or resolution of clinical signs
      – 73% antigen negative
    • Resolved pulmonary inflammation sooner than 3-D melarsomine alone
    • 3-D melarsomine alone resulted in faster killing of adults
Designing Practical Protocols

- Understand the Evidence - Doxycycline
  - *Wolbachia pipientis*
    - Bacterial endosymbiont of *D. immitis*
  - Responsible for
    - Parasite embryogenesis
    - Larval development
    - Microfilarial production
    - Long-term survival of adult worms
    - Depresses host immune system

- Use with preventive reduces microfilarial count within 3 months
- Weekly ivermectin + intermittent doxycycline
  - Faster decrease in mf count and higher adulticide efficacy at 36 weeks vs. ivermectin or doxycycline alone
- Doxycycline (30d)
  - Eliminates L3, L4 and juvenile worms
  - Delays mf production
- Mosquitos fed on blood from dogs treated with doxycycline produced non-infective L3

- Surviving worms continue to damage pulmonary vasculature
- Exercise restriction must be maintained
Designing Practical Protocols

• Mitigate the Risks
  – Prescribe treatment based on disease severity
    • No clinical signs → 2-dose protocol
    • Clinical signs → 3-dose protocol
  – Utilize adjunctive treatments
    • Doxycycline → Always
    • Prednisone → Circulating mf, clinical signs
  – Consider alternative protocols (doxycycline + ivermectin)
    • No clinical signs
    • LOS is less important (e.g., sanctuary, foster)
    • Melarsomine shortage
    • Opportunity for informed adoption

Conclusions

• Heartworm disease is an issue of increasing importance to veterinarians, animal shelters, and adopters
• Shelters are faced with many challenges to following standard guidelines
• When necessary, steps can be taken to mitigate risk of suboptimal management protocols

FAQ’s

• Do I spay/neuter before or after heartworm treatment?
  – UF Veterinary Community Outreach Program
    • ~100 treatments per year
    • Spay-neuter before or 4-6 weeks after
    • No peri-operative complications attributed to HW status
  – 2013 Triennial Heartworm Symposium
    • No increase in perioperative complications in dogs with no to mild clinical signs of disease
FAQ’s
• What can I use in place of doxycycline?
  – Minocycline
  – Azithromycin
  – Custom compounding
  – Rifampin effective against Wolbachia in other filarial worms
  – Avian/aquatic formulations

FAQ’s
• Melarsomine administration

Wags 4 Hope

Annie Blumenfeld, wags4hope@gmail.com
References


