Heartworm infections, which are caused by *Dirofilaria immitis*, were first noted in 1921. *D. immitis* has been shown to infect a wide variety of animal species, including dogs, cats, ferrets, foxes, wolves, sea lions, and horses. The distribution of the disease is mainly affected by the distribution of the reservoir (canine species). The number and feeding pattern of different mosquito species influence the prevalence of heartworm disease in each local niche. The infection is entirely preventable with safe, inexpensive products. Treatment of infected dogs can be expensive, and the complications are potentially life threatening. The effects on the lungs are often irreversible.

**DIAGNOSTIC CRITERIA**

**Historical Information**

**Gender/Age/Breed Predisposition**
- None.

**Owner Observations**
- Exercise intolerance.
- Coughing.
- Cachexia.
- Anorexia.

**Other Historical Considerations/Predispositions**

Dogs are highly susceptible to heartworm infection. Experimentally, nearly 100% of dogs exposed to mosquitoes carrying infective larvae develop adult heartworms. In endemic areas, the mongrel and wild canine (coyotes) populations, which are not presented for veterinary care, often serve as the key reservoir population harboring microfilariae for mosquitoes.

**Physical Examination Findings**
- Sedentary dogs may be asymptomatic regardless of worm burden.
- Labored breathing, dyspnea, and/or rales.
- Tachycardia.
- Cachexia.
- Heart murmur (audible third heart sound).
- Ascites.

**Laboratory Findings**
- **Positive antigen test**: Dogs must have fully mature female heartworms present to test positive (which occurs more than 6 months after infection).
- **Positive Knott's test**: 40% of dogs with adult heartworm infections will test negative.
- **Microfilariae**: Noted on concentration tests.
- **Eosinophilia and basophilia**: Inconsistently present.
- **Inflammatory leukogram**.
- **Thrombocytopenia**: Associated with thromboembolic disease and especially heartworm death. Platelet counts may drop significantly (<100,000/µl) after initiating adulticidal therapy.

**Also in this issue:**

7 Ferret Cardiomyopathy
• **Anemia:** Extent depends on the chronicity and severity of the disease and thromboembolic complications; more typical of postcaval disease.

• **Proteinuria:** Seen in animals with severe and chronic infection; thought to be caused by immune-complex glomerulonephritis. Most dogs with severe proteinuria based on protein:creatinine ratio have irreversible glomerular disease, even if adult heartworms are eliminated.

### Other Diagnostic Findings

#### Thoracic radiography: $$
- Enlarged, tortuous, truncated peripheral intra- and interlobar branches of the pulmonary artery, particularly in the diaphragmatic lobes.
- Variable degrees of pulmonary parenchymal disease.
- Right-sided heart enlargement (reverse “D” on ventrodorsal radiographs) with a pulmonary arterial bump at the 1-o’clock position if the dog has been active.

#### Echocardiography: Allows definitive diagnosis and assessment of heart changes. $$
- Does not always detect adult heartworms; unable to visualize the peripheral branches of the pulmonary arteries.
- Visualization of heartworms (parallel, linear echo densities) in the right ventricle, right atrium, and pulmonary arteries.
- Useful to confirm a diagnosis of caval syndrome in heartworm-positive dogs with an audible murmur and ascites.

#### Electrocardiography: $$
- Most sedentary dogs have a normal electrocardiogram.
- Active dogs may demonstrate a right axis shift due to hypertrophy of the right ventricle.

### Summary of Diagnostic Criteria

#### History:
- Lack of heartworm prevention or lapse in monthly prevention for more than 2 months in succession.
- Exercise intolerance.
- Coughing.
- Anorexia.

#### Physical examination: Patient may be asymptomatic, or the following may be noted:
- Labored breathing/dyspnea.
- Tachycardia.
- Heart murmur.
- Ascites.

#### Positive antigen test and/or microfilaria test.

### KEY TO COSTS

<table>
<thead>
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<th>Cost Symbol</th>
<th>Description</th>
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</tr>
<tr>
<td>$</td>
<td>costs over $1,000</td>
</tr>
</tbody>
</table>
• Thoracic radiography:
  — Enlarged tortuous pulmonary arteries.
  — Right-sided heart enlargement.
• Laboratory findings are usually normal, but the following may be noted:
  — Eosinophilia.
  — Thrombocytopenia.
  — Anemia.
  — Proteinuria.

Diagnostic Differentials
• Causes of pulmonary hypertension and thrombosis:
  — Hyperadrenocorticism.
  — Glomerulonephritis and/or amyloidosis.
  — Immune-mediated hemolytic anemia (IMHA).
  — Disseminated intravascular coagulation (DIC).
  — Chronic obstructive pulmonary disease (COPD).
  — Neoplasia.
  — Pancreatitis.
  — Sepsis.
• Allergic lung disease.
• Other lung parasites, most likely the French heartworm (Angiostrongylus vasorum).
• Causes of ascites:
  — Right-sided heart failure.
  — Liver failure.
  — Pericardial disease.
  — Dilated cardiomyopathy.
  — Hypoproteinemia.
  — Ruptured bladder.
  — Peritonitis.
  — Neoplasia.
  — Hemorrhage.

TESTING GUIDELINES

Important Note: If prophylactic medications for heartworms are initiated in any dog older than 4 months of age, antigen testing to detect adult heartworms, which were immature at the time the preventive program was initiated, is necessary 3 to 4 months after initiation of the preventive. If the test is not performed until 1 year after the initiation of a preventive protocol, it is not possible to discern whether a positive test result is due to infection with immature worms at the time the preventive was initiated, failure of the product, or lack of owner compliance.

ON THE NEWS FRONT
— *Wolbachia* is a bacterium that appears to be an endosymbiont of *Dirofilaria*. This intracellular organism is found in all stages of the life cycle (microfilariae, L1–3 in mosquitoes and L3–5 in animals) but is more numerous in mature female heartworms. Heartworms need *Wolbachia* to maintain the ability to reproduce, and treatment with tetracyclines has resulted in sterile heartworms.

— The clinical effect of coinfections with *Wolbachia* in the immunologic response of dogs with heartworm infestations is open for debate. Based on the genome of the bacterium, no endotoxin is associated with *Wolbachia*. Antigen from the bacterium can be found in many of the host animal’s organs (e.g., kidney, liver).

Antigen Testing
• Antigen testing is the most specific diagnostic method, with microwell testing being the most sensitive method in low-antigen antigenemia.
• Antigenemia will not appear for 6 to 7 months after infection.
• Antigen tests consistently have a high specificity.
• The amount of antigen in circulation bears a direct, but imprecise, relationship to the number of mature female heartworms.
• False-positive results are most commonly due to technical error.
• False-negative results may be due to:
  — Low worm burden.
  — Immature worms (which may already be in the pulmonary arteries).
  — Presence of only adult male heartworms.

Microfilaria Testing
• Approximately 40% of heartworm-infected dogs may not have microfilariaemia.
• When conducting a microfilaria evaluation, a minimum of 1 ml of blood should be examined using a concentration technique.
• Microfilariaemia does not appear until 6 to 7 months after infection.
• Three percent of dogs with *D. immitis* microfilariae will not have adult heartworms in the heart. Adult heartworms may die, leaving microfilariae in circulation, and microfilariae from an infected bitch can cross the placenta and be present in the blood of puppies at birth.
It is important to distinguish between *D. immitis* and *Dipetalonema reconditum* (Table 1).

### Changing Chemoprophylaxis Products

Dogs should be tested before changing to a new product and then retested 4 months after initiation of the new product. This evaluates the efficacy of the original product as well as owner compliance.

### ADULTICIDAL TREATMENT RECOMMENDATIONS

#### Initial Treatment $-$ $^\S$

- A diagnosis of heartworm infection should be reconfirmed, and testing should include an estimate of antigen load via a microwell titer test.
- Heartworm prevention should be initiated with a product that does not rapidly kill microfilariae at its preventive dose. If no microfilariae are found, milbemycin oxime (Interceptor, Novartis Animal Health) may also be used at this time. Administration of a heartworm preventive prevents additional infections from developing while the dog is being treated for the current infection.
- Clinically ill animals should be stabilized before treatment.
  - Cardiovascular support: IV fluid therapy. Central venous pressure should be measured because right-sided heart failure and lung inflammation can become critical when administering IV fluids.
  - Respiratory support: Oxygen.
- The organoarsenical adulticide melarsomine (Immiticide, Merial; 2.5 mg/kg via deep IM injection into the epaxial lumbar muscles) is the only heartworm adulticide approved for use in dogs.
- There may be some swelling and/or soreness after administration.
- Determining the stage of heartworm disease based on clinical signs and radiographic changes can be misleading. Sedentary dogs that harbor large worm burdens may have minimal radiographic changes and no clinical signs. The compilations of heartworm adulticidal therapy are directly related to the number of heartworms killed; thus, a patient with a high antigen load should be treated cautiously regardless of clinical signs. Likewise, a low antigen load may mask a large number of males and/or immature worms, which will also be killed. This is an important consideration because treatment recommendations cannot be based on clinical signs or radiographic changes as such findings are not always representative of the worm burden.
- **Standard protocol:** Two injections separated by 24 hours.
  - May be used in dogs with a low risk of pulmonary thromboembolism (i.e., those with a low worm burden).
  - Strict exercise restriction for 4 to 6 weeks after treatment is vital to prevent pulmonary thromboembolism.
- **Alternative (two-stage) protocol:** One dose followed by the standard two-injection protocol 4 to 6 weeks after the initial injection. This protocol is safest in high-risk patients (less risk of pulmonary thromboembolism) and is recommended by the American Heartworm Society. The initial dose kills approximately 30% of worms; the remaining adult heartworms are killed after administration of the latter injections 24 hours apart. However, if the worms present are older, even a single dose can result in severe pulmonary

### CURRENTLY AVAILABLE HEARTWORM PREVENTIVES

- Heartgard (ivermectin): Merial
- Heartgard Plus (ivermectin and pyrantel): Merial
- Interceptor (milbemycin oxime): Novartis Animal Health
- Iverhart Plus (ivermectin): Virbac
- Revolution (selamectin): Pfizer Animal Health
- Sentinel (milbemycin oxime and lufenuron): Novartis Animal Health
- Tri-Heart Plus (ivermectin): Schering-Plough Animal Health

<table>
<thead>
<tr>
<th>Type of Sample</th>
<th><em>Dirofilaria immitis</em></th>
<th><em>Dipetalonema reconditum</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh smear</td>
<td>Few to large numbers</td>
<td>Usually small numbers</td>
</tr>
<tr>
<td></td>
<td>Undulate in one place</td>
<td>Move across fields</td>
</tr>
<tr>
<td>Stained smear</td>
<td>Straight body</td>
<td>Curved body</td>
</tr>
<tr>
<td></td>
<td>Straight tail</td>
<td>Posterior extremity</td>
</tr>
<tr>
<td></td>
<td>Tapered head</td>
<td>Hook</td>
</tr>
<tr>
<td></td>
<td>&gt;290 µm long</td>
<td>&lt;275–280 µm long</td>
</tr>
<tr>
<td></td>
<td>&gt;6 µm wide</td>
<td>&lt;6 µm wide</td>
</tr>
</tbody>
</table>

#### TABLE 1

*Dirofilaria immitis* versus *Dipetalonema reconditum*
signs. Strict exercise restriction continues to be vitally important throughout the treatment period.

- Complications noted with adulticidal treatment are relative to the number of heartworms present and the rapidity of worm death.
- Antigen tests should be performed 4 to 6 months after treatment to evaluate treatment efficacy. If the dog is still antigen positive, it may simply need more time to seroconvert and should be retested in another 1 to 2 months.
- For dogs diagnosed with caval syndrome (heartworms obstructing the blood flow though the tricuspid valve, interfering with valve closure; characterized by severe passive congestion of the liver, jugular pulses, sudden onset of lethargy and weakness, hemoglobinemia, and hemoglobinuria), surgical correction via physical removal of the heartworms is the treatment of choice, followed by adulticidal treatment several weeks later.

**Alternative/Optional Treatments/Therapy**

**Prophylactic Doses of Ivermectin with Pyrantel Pamoate**

- Effective against precardiac larvae and young adults (i.e., when administered sooner than 7 months after infection and given continuously for 1 year).
- Moderately effective as an adulticide if given for longer than 1 to 2 years continuously.
- **Note:** It cannot be assumed that dogs will be cleared of adult heartworms with this therapy. This approach does not prevent the ongoing damage caused by the presence of adult heartworm(s), and damage from worm death may produce additional lung damage. Because the time of worm death cannot be predicted, severe lung damage may occur in active dogs.

**“Reach-Back” Effect of Monthly Preventives**

Although year-round use of monthly preventives can decrease the adult worm burden when administration is started no more than 3 months after the infection, this therapy simply kills immature heartworms in the pulmonary arteries and lungs and thus is not a true preventive. Rather, it simply provides a safety net by eliminating immature and young adult heartworms over 12 to 18 months. Death of the immature heartworms results in lung injury, and the timing of the injury is directly related to the worms dying in the pulmonary arteries and associated lung pathology.

**Supportive Treatment**

- Strict exercise restriction is vitally important during treatment and for 4 to 6 weeks afterward to minimize the chance of complications seen with acute lung injury associated with heartworm death.
- IV fluids may be necessary in animals that become critically ill after being treated for heartworms. Central venous pressure should be monitored to avoid overloading the right ventricle and compromised lung.
- Acute lung injury associated with heartworm death may be treated with 24 hours of high-dose, short-acting corticosteroids (prednisolone sodium succinate [Solu-Delta Cortef, Pfizer Animal Health]; 2–4 mg/lb IV; frequency depends on response to treatment).
- If dogs develop DIC secondary to worm death, treatment to counter the effects of DIC must be initiated. Thrombocytopenia without DIC is common with massive worm death, and a low platelet count alone does not warrant a diagnosis of DIC or a poor prognosis.

**Patient Monitoring**

- Antigen and microfilaria tests should be performed 4 to 6 months after treatment to evaluate the efficacy of adulticidal therapy.
- Thoracic radiographs should be reviewed to assess cardiovascular and pulmonary changes.

**SUMMARY OF DIAGNOSTIC STEPS AND TREATMENT**

- Positive antigen tests should be confirmed with a microwell test, which allows the antigen load to be estimated.
- A complete blood test, chemistry panel, and urinalysis are indicated to detect subclinical disease.
- Thoracic radiography reveals enlarged tortuous pulmonary arteries and right-sided heart enlargement.
- Preventive medication with a nonmicrofilaricidal agent should be initiated at the time of diagnosis.
- Adulticidal treatment should be initiated (one injection of melarsomine [2.5 mg/kg]), and exercise should be restricted for 4 weeks.
- Four weeks later, two additional injections of melarsomine are given 24 hours apart, and exercise should be restricted for an additional 4 to 6 weeks.
- Antigen testing and testing for the presence of microfilariae should be done 4 months after adulticidal treatment has been completed. If microfilariae are present, microfilaricidal treatment with ivermectin (50 µg/kg) or preventive doses of milbemycin oxime (0.5 mg/kg) should be initiated.
associated with heartworm presence and response to treatment. The lung pattern often demonstrates severe pulmonary parenchymal edema and not actually obstruction of blood flow or infarction.

- Platelet count should be evaluated in patients that become dyspneic or tachypneic. If the platelet count is below 100,000, DIC should be considered and fibrin degradation products and a coagulation profile should be evaluated.
- Nasal oxygen is always recommended, and pulse oximetry should be used to determine the severity of the lung injury.

**Home Management**

- The most important step in controlling heartworm disease in a region is to decrease the reservoir animals (elimination of the microfilaria source for mosquitoes). Prevention can easily be accomplished by initiating heartworm preventive in dogs at 4 months of age.
- Although heartworm disease is typically not transmissible for several months of the year depending on local climate, year-round prevention is advisable to increase owner compliance and provide retroactive efficacy as a safeguard for occasional missed doses; in addition, many of the heartworm preventives also control other endo- and ectoparasites.

**Treatment Contraindications**

- Caval syndrome patients: Adulticidal treatment should be delayed until after heartworms have been surgically removed.
- Systemically ill (critical) patients: Treatment may be worse than the disease.

**PROGNOSIS**

**Favorable Criteria**

- Low worm burden.
- Systemically healthy patient.
- Absence of cardiac or respiratory changes.

**Unfavorable Criteria**

- Caval syndrome.
- Systemic illness.
- Glomerulonephritis.

**RECOMMENDED READING**

