Treating Heartworm Infection
Ancillary Corticosteroid Therapy in Dogs
Clarke Atkins, DVM, Diplomate ACVIM (Internal Medicine & Cardiology)

The Heartworm Hotline column is cosponsored by Today’s Veterinary Practice and The American Heartworm Society (heartwormsociety.org). This series presents questions and answers on topics related to heartworm infection, prevention, diagnostics, and/or treatment.

QUESTION
In the July/August 2012 Heartworm Hotline article—Doxycycline in the Management of Heartworm Disease—the role of doxycycline in the medical management of heartworm infection was discussed. What about other drugs? For example, when would you employ corticosteroids, aspirin, and NSAIDs?

ANSWER
In my opinion, steroids and nonsteroidal anti-inflammatory drugs (NSAIDs) have a definite, but restricted role in the treatment of heartworm disease (HWD) in dogs. This article will discuss use of corticosteroids; the next article will examine the role of NSAIDs.

ROLE OF CORTICOSTEROIDS
The anti-inflammatory and immunosuppressive effects inherent to corticosteroids are therapeutic for some aspects of HWD. I make the disease versus infection distinction because I see almost no role for corticosteroids in heartworm infection (HWI) unaccompanied by clinical signs (see Heartworm Infection versus Heartworm Disease, page 86).

In general, this class of drugs is indicated in HWD for:
• Pulmonary parenchymal complications
• Treatment or prevention of adverse reactions to microfilaricides and adulticides.

However, each patient is an individual and corticosteroids are not a benign therapy. Therefore, it is important that practitioners evaluate each unique case, weighing the pros and cons, to decide whether corticosteroids should be part of their treatment protocols.

CORTICOSTEROIDS IN DOGS WITH HEARTWORM INFECTION
In heavily endemic areas, practitioners assume heavy heartworm burdens and often pretreat infected dogs with corticosteroids, prior to and during adulticidal therapy.

The American Heartworm Society’s position on administering ancillary steroid therapy prior to adulticide is: In highly endemic areas, where animals are more likely to have significant worm burdens, glucocorticoids, such as prednisone may be used. This is far from a ringing endorsement for use of corticosteroids in asymptomatic canine patients and has geographic limitations in terms of heartworm prevalence.

I do not advocate the use of corticosteroids to treat chronic HWI in dogs with no clinical signs of disease or little to no risk for developing significant pulmonary complications. In my opinion, chronic corticosteroid therapy in HWI to reduce pulmonary vascular lesions is contraindicated.

CORTICOSTEROIDS IN DOGS WITH HEARTWORM DISEASE
Therapeutic Use For Pulmonary Complications
Allergic pneumonitis (pulmonary infiltrate with eosinophils, eosinophilic pneumonitis), thought to result from microfilariae destruction in the lungs, is very steroid-responsive. It is characterized by cough and
variable dyspnea, interstitial to alveolar pulmonary infiltrates on radiographs, and eosinophilic airway cytology.

- Prednisone or prednisolone (1 mg/kg Q 24 H) is administered for 3 to 5 days and discontinued or tapered as clinical conditions allow. 1,2,8
- Prednisone/prednisolone tapering has been advocated at:
  - 0.5 mg/kg Q 12 H to complete the first week of treatment
  - 0.5 mg/kg Q 24 H the second week
  - 0.5 mg/kg every other day for the third and fourth weeks.

The response is generally favorable, but it may be necessary to treat for a more protracted period of time if recurrence of cough and/or tachypnea/dyspnea is noted upon tapering. If anti-inflammatory treatment is needed for an extended time, I suggest administration Q 48 H as long as clinical signs can be kept in abeyance. Typically, such extended therapy is not necessary.

**Eosinophilic granulomatosis**, a more serious but rare manifestation of HWD responds less favorably to prednisone. It is characterized by a more organized, nodular eosinophilic inflammatory process, associated with bronchiolalymphadenopathy and, occasionally, pleural effusion. 2,8,9 With pulmonary granulomatosis, cough, wheezes, and pulmonary crackles are often audible; when HWD is very severe, lung sounds may be muffled and associated with dyspnea and cyanosis.

Treatment with prednisone at twice the dosage for allergic pneumonitis is reported to induce partial or complete remission in 1 to 2 weeks.

- The prognosis remains guarded because recurrence within several weeks is common.
- Prednisone may be combined with cyclophosphamide (50 mg/m² PO Q 24 H for 4 days for dogs; ensure adequate diuresis due to risk of sterile cystitis) or azathioprine (1.65–2.2 mg/kg PO Q 24–48 H for dogs) in an effort to heighten the immunosuppressive effect. The latter combination appears to be the most effective.
- Adulticide therapy should be delayed until remission is attained.
- Because the prognosis for medical success is guarded, surgical excision of lobar lesions has been advocated. 6,9

**Pulmonary thromboembolism** (PTE), an acute lung injury, usually follows administration of adulticide, typically by 7 to 21 days as adult worms die and disintegrate. This is particularly true if the dog is allowed to exercise during the first 30 to 45 days after treatment. PTE also occurs unrelated to adulticidal treatment, presumably due to spontaneous worm death.

Prednisone (1 to 2 mg/kg Q 24 H) has been advocated, along with cage rest, oxygen if needed, and supportive care, in the management of PTE; therapeutic care is continued until radiographic and clinical improvement is noted. 1,4,10

When using corticosteroids in dogs with PTE, note the following cautions:

- Due to the potential for steroid-induced fluid retention (mineralocorticoid effect), such therapy should be used cautiously in the presence of heart failure or impending heart failure.
- PTE may precipitate heart failure by structural and functional occlusion of pulmonary arteries (the latter due to resultant vasoconstriction), contributing to elevated pulmonary artery pressures and right ventricular afterload.
- Early studies demonstrated that postadulticidal corticosteroid therapy reduced pulmonary blood flow and made intimal disease worse in a model of HWD. 4 Corticosteroids are procoagulant, possibly more so when used in conjunction with adulticides, therefore potentially exacerbating pulmonary thromboembolism. 4

### Indications for Corticosteroid Therapy in Dogs with Heartworm Disease

- To treat pulmonary parenchymal complications:
  - Pulmonary eosinophilic infiltrates
  - Eosinophilic granulomas
  - Pulmonary thromboembolism (spontaneous or postadulticide)
- To prevent or treat adverse reactions to treatment:
  - Minimize or prevent adverse reactions to microfilaricidal therapy with macrocyclic lactones
  - Minimize or prevent adverse reactions to adulticides (particularly PTE)
  - Reduce local reactions to melarsomine

### Prevention of Adverse Reactions to Treatment

**Adverse Reactions to Microfilaricides**

Despite the fact that no agent is approved by the Food and Drug Administration for the elimination of microfilaria, microfilaricidal therapy has traditionally been instituted 3 to 6 weeks after adulticide administration. 1,11,12 However, I agree with the protocol now advocated by the American Heartworm Society: Preventives should be instituted at time of diagnosis, with resultant gradual decline in microfilarial numbers.

Macrolides offer a safe and effective alternative to levamisole and dithiazanine, which were historically used for this task. Microfilariae are rapidly cleared with:

- Ivermectin at 50 mcg/kg (approximately 8× the preventive dose) 11 or

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**Heartworm Infection versus Heartworm Disease**

- **Heartworm infection** indicates that the patient is parasitized by at least one life stage of the heartworm. Animals with HWI typically have no radiographic or clinical signs of disease.

- **Heartworm disease** affects patients with HWI. These animals manifest radiographic and/or clinical signs of HWD.
WHAT THE DATA TELL US
Prednisone, the steroid most often prescribed for canine patients, and prednisolone, which is substituted for use in feline and some canine patients, have demonstrated variable results in heartworm-transplant models of HWD. These models evaluated the effect of worm death on the host, using either dead worms or canine recipients that received the arsenical thiacetarsamide.

Conflicting results (Table) regarding the effect of corticosteroids on arsenical efficacy and HWD complications, warrant, at the very least, caution when deciding whether to prescribe corticosteroids in an effort to reduce adverse reactions following adulticidal therapy. This is particularly true when using the 2-dose method as the small study showing absence of steroid-induced reduction in melarsomine efficacy used the 3-dose protocol.

To read more about adulticidal therapy, including 2-dose versus 3-dose methods, read Doxycycline in the Management of Heartworm Disease in the July/August 2012 issue of Today’s Veterinary Practice available at todaysveterinarypractice.com.

TABLE. Studies of Corticosteroid Use in Heartworm Disease

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<tr>
<th>ADVANTAGES</th>
<th>LIMITATIONS</th>
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<td>Corticosteroids diminished the severity of pulmonary eosinophilic infiltrate related to heartworms and arteritis and periarteritis induced by dead worms.</td>
<td>No reduction in melarsomine’s adulticidal efficacy with concurrent steroid therapy has been documented; a small (n = 5) study, using the “split” 3-dose melarsomine regimen and tapering dosage of prednisone, showed a 100% kill rate for transplanted worms.</td>
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<td>Two studies documented a reduction in adulticidal efficacy when thiacetarsamide was used concurrently with corticosteroids.</td>
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- Milbemycin at 500 mcg/kg (preventive dose). Note that these recommendations represent an extra-label use of ivermectin.
- Adverse reactions, the severity of which is likely related to microfilarial numbers, were observed in 6% of 126 dogs receiving ivermectin at the microfilaricidal dose. Dogs less than 16 kg, with more than 10,000 microfilaria/mL blood, were more apt to suffer adverse reactions.
- Signs included shock, depression, hypothermia, and vomiting.
- With fluid (shock dosage) and corticosteroid (high-dose dexamethasone) therapy, all dogs recovered within 12 hours.
- One fatality, however, was observed 4 days after microfilaricidal therapy.
- Similar findings and frequency were reported with milbemycin administration at the preventive dose. Dogs treated with fluid and corticosteroid therapy should be hospitalized and carefully observed.
- Administer: Benadryl (2 mg/kg IM) plus Dexamethasone (0.25 mg/kg IV) or Prednisone/prednisolone (1 mg/kg PO 1 H prior to and 6 H after first macrolide dose) prophylactically to prevent adverse reactions to microfilaricidal doses of macrolides.

Adverse Reactions to Adulticides
Adverse effects of adulticides are primarily related to the risk of pulmonary thromboembolism caused by dead worms. Tapering doses of prednisone can be administered, starting at the time of each melarsomine injection, as follows:

- First week: Prednisone, 0.5 mg/kg PO Q 12 H
- Second week: Prednisone, 0.5 mg/kg PO Q 24 H
- Third & fourth weeks: Prednisone, 0.5 mg/kg PO every other day.

Local Tissue Reaction to Melarsomine
Local inflammation is the most common reaction to an intramuscular injection of melarsomine. This is characterized by pain, swelling, and persistent hard lumps at the injection site, accompanied by muscle stiffness and unwillingness to move.

This inflammation can be minimized by careful injection of the drug deep into the belly of the epaxial muscle. Additionally, a short course of anti-inflammatory doses of corticosteroids, given at the time of injection, decreases the likelihood of a local reaction without affecting melarsomine’s efficacy.

CORTICOSTEROID CAUTIONS
Side effects of corticosteroid administration include polyuria/polydipsia, hypercoaguability, immunosuppression, diabetes mellitus, iatrogenic Cushing’s syndrome, psychological changes, muscular wasting, and endocrinologic and dermatologic abnormalities.

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TWENTY QUESTIONS FOR CHECKING REFERENCES

1. What is the name and position of the person providing the information on the candidate?
2. What were the start and end dates of the candidate’s employment?
3. What was the candidate’s job title, duties, and responsibilities?
4. What was the candidate’s starting and ending salary?
5. Why did the candidate leave?
6. Is the candidate eligible for rehire? (If the previous employer says no because the company’s policy is not to rehire, ask whether he or she would rehire if that policy didn’t exist.)
7. After you briefly describe the position you are looking to fill, does the previous employer think the candidate would be successful in this position?
8. Was the employee honest and did he/she have integrity?
9. Did the candidate arrive for work on time?
10. Was the candidate absent an excessive amount of time?
11. What was the candidate’s quality of performance?
12. What were the candidate’s strengths and weaknesses?
13. Did the candidate work well with clients and other staff?
14. Was the candidate able to work well independently?
15. Did the candidate possess satisfactory technical/computer skills?
16. Did the candidate have supervisory duties?
17. What were the duties and how well were they performed?
18. Did the candidate advance at the company?
19. What promotions did he/she receive?
20. Is there any other information that would be useful in making an employment decision?

Karen E. Felsted, CPA, MS, DVM, CVPM, is the owner of Felsted Veterinary Consultants, Inc, which offers business consulting to both private practices and the animal health industry. She is the treasurer for VetPartners (vetpartners.org) and the CATalyst Council (catalystcouncil.org) as well as a member of the Certified Veterinary Practice Manager (CVPM) board of directors (vhma.org). She previously served as the CEO for the National Commission on Veterinary Economic Issues (ncvei.org). In 2011, she received the Western Veterinary Conference Practice Management Continuing Educator of the Year award. She received her BA in marketing from University of Texas at Austin, her MS from University of Texas at Dallas, and her DVM from Texas A&M University. She practiced small animal and emergency medicine while maintaining a veterinary accounting and consulting practice. She has also provided services to Brakke Consulting, Inc, and Gatto McFerson CPAs, a veterinary-focused financial and consulting firm.

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Avoiding side effects is important; therefore, corticosteroids should be used at the lowest dosage possible. After successful resolution of the treated problem, they should be discontinued gradually. If the clinical situation does not allow tapering the dosage to zero, using the lowest dosage possible, every other day, is a relatively safe alternative.

HWD = heartworm disease; HWI = heartworm infection; NSAID = nonsteroidal anti-inflammatory drug; PTE = pulmonary thromboembolism

References


Clarence Atkins, DVM, Diplomate ACVIM (Internal Medicine & Cardiology), is the Jane Lewis Seaks Distinguished Professor of Companion Animal Medicine at North Carolina State University. He is also a member of the Today’s Veterinary Practice Editorial Peer Review Board and American Heartworm Society’s Executive Board. Dr. Atkins received the 2004 Norden Award for excellence in teaching. His research involves canine and feline heartworm disease and pharmacologic therapies for cardiac disease. Dr. Atkins received his DVM from University of California–Davis and completed his internship at Angell Memorial Animal Hospital in Boston, Massachusetts.