Notes on management of heartworm infection when animals are transferred from endemic to non-endemic areas

Note that the following are intended as informational guidelines only. These are not definitive: many reasonable choices exist depending on the resources and constraints affecting any given shelter.

A. **Use of preventive products in heartworm negative dogs:** Some dogs may have been on heartworm preventive until the time of the hurricane, but probably missed treatment since being lost. Resuming preventive treatment [such as low-dose-ivermectin (HeartGard® and related products), milbemycin (Interceptor® and related products) and selamectin (Revolution®)] now will ensure that a recently acquired infection will be eliminated before progressing. Retroactive efficacy ("Reach back") for all products is assured for one month, and may be effective for as long as three or four months post-infection.

B. **Suppression of microfilariae in dogs with heartworm infections:** Many of the hurricane refugee dogs already have well established heartworm infections and have circulating microfilaria. According to the guidelines of the American Heartworm Society, "preventive" therapy should be initiated as soon as a heartworm infection is diagnosed. There will be a gradual to precipitous drop in microfilariae in the blood of all the treated dogs within a few days of treatment depending on the treatment used, but not all microfilariae will be eliminated from the circulation of some dogs. All dogs treated with Heartgard or Milbemycin in the studies discussed below still had circulating microfilariae present in the blood following a single treatment, and almost all the dogs had circulating microfilariae present after 2 monthly treatments.[2] There may be an increased risk of adverse reactions when Milbemycin is used in dogs with high levels of circulating microfilaria, due to more rapid die-off.

   An oral dose of 50 micrograms per kilogram ivermectin may effectively suppress microfilaremia in all dogs until the heartworms can be removed. See below for information on diluting ivermectin.[4] This dose is based on post-treatment guidelines that were in place before the current monthly product were available. Although this regimen has not been tested like the above products for suppression of microfilaremias, it is likely that the higher dose of ivermectin will induce clearance in more animals. However, the resulting massive die off of microfilaria is more likely to lead to adverse reactions than the low dose treatment, including potential anaphylaxis and death. This is particularly likely in dogs with high levels of circulating microfilaria. Neither clinical signs nor the strength of positive on a heartworm ELISA test can predict the degree of microfilaremia, but given the high level of endemic heartworm disease in the area where many of the rescued dogs originated, it is prudent to assume that high levels are common.

   i. **Reasonable compromise for microfilaricidal treatment:** In areas where mosquitoes are not a threat at this time of year, or where most dogs are

likely on preventive treatment due to endemic disease, rapid microfilaricidal treatment is not a priority and preventive level ivermectin (6 micrograms/kg, e.g. Heartgard ®) is adequate. For those areas where transmission *is* a concern, an approach which would minimize the risk of adverse reactions in the rescue dogs while providing a reasonably rapid clearance of microfilaremia would be to administer two doses of preventive level ivermectin two weeks apart, followed two weeks after the second low dose with a higher dose of 50 micrograms/kg ivermectin PO.

ii. **Monitoring after microfilaricidal treatment:** Dogs should be monitored for at least 8 hours after treatment. Signs of adverse reactions include: lethargy, inappetence, salivation, retching, pale mucous membranes, tachycardia and acute circulatory collapse. Treatment of adverse reactions includes fluid support and 1-2 shock doses of steroids. Pretreatment with injectable prednisone 1 mg/kg and diphenhydramine 1 mg/kg may reduce the risk of adverse reactions.

C. **Adulticidal treatment:** All heartworm positive dogs should be treated with adulticidal therapy within 6 months of diagnosis. Although monthly treatment with preventive doses of ivermectin has been effective in clearing some early infections, this *can not be relied upon.* Many of these dogs will have much heavier infections than we are used to seeing in most parts of the United States, and are at consequently higher risk for pulmonary thromboembolism post-treatment. Full pre-treatment workup includes both antigen and microfilaria test, chest radiographs, complete blood count, blood chemistry and urinalysis. Although individual adopters or foster parents may elect this route, it is likely financially prohibitive when treating large numbers of dogs with heartworm. The main purpose, aside from the prognostic value, is to determine whether to a 2 or 3 dose melarsomine (immiticide®), treatment regimen is required. The cost of the additional treatment may be less than the pretreatment workup, and it is probable that most dogs will require the 3 treatments anyway. The American Heartworm Society recommends the 3 dose treatment regimen as the treatment of choice in *all* dogs due to increased safety and efficacy.

i. **Reasonable compromise for adulticidal treatment:** A reasonable compromise would be to forego the pretreatment workup and simply treat all dogs with a single dose of melarsomine followed 1 month later by 2 doses, 24 hours apart. The risk of thromboembolic disease may be reduced if dogs are treated with a preventive product for 3 months *prior* to adulticidal therapy. Treatment with a tapering dose of prednisone (.5 mgs/kg BID x 1 week, SID x 1 week, then EOD x 1 week) following each injection of melarsomine may also be helpful. All dogs must be strictly cage rested between injections and for thirty days after the second set of injections. It should be recognized that many of these dogs are at very high risk, and some adverse reactions should be expected despite every precaution.

D. **Risk of infection to other dogs:** The concern has been raised that transport of heartworm positive dogs will introduce disease into non-endemic areas. It should be recognized that traffic of dogs in and out of endemic areas is a common occurrence in our highly mobile society, and heartworm disease is often recognized even in so called non-endemic areas. However, it is true that more dogs will not be on preventive products in areas normally considered low risk. If a suitable mosquito vector is present, has access to a heartworm infected dog with circulating microfilaria, and subsequently lives long enough to permit development of larvae to an infective stage, dogs not on preventive product would be vulnerable to infection.

E. **Minimizing risk:** In order for infection to be transmitted, a mosquito must bite a microfilaremic dog, then survive long enough for larvae to mature (at least 10-14 days at average temperatures of 80 degrees F). When temperatures drop below 57 degrees F for a few hours or more per 24 hour period, maturation of larvae may take even longer. Mosquito control and prompt administration of microfilaricidal treatment as described above will minimize any risk of transmission. As an additional precaution, all dogs housed in the same environment (foster home or shelter) should be on preventive treatment unless it is *certain* that no mosquitoes are present due to climatic considerations.

F. **Spay/neuter surgery of heartworm positive dogs:** Many of the dogs rescued from the hurricane aftermath are intact. Shelters may face legal, logistical and ethical constraints regarding releasing these intact dogs to foster homes and adopters. Some veterinarians experienced in working with heartworm positive dogs report a preference for spaying and neutering heartworm positive dogs *prior to treatment* provided the dog is not in heart failure. If not altered prior to treatment, it may be preferable to delay surgery until 60 days after adulticidal treatment.[3] If the more conservative treatment approach outlined above is followed (3 months on prophylactic followed by split dose immiticide treatment) this would mean delaying surgery by a minimum of 6 months, creating a significant risk of unwanted puppy production as well as difficulties in follow-up. If surgery is performed prior to adulticidal treatment, caution should be exercised to avoid fluid overload. Any standard anesthetic protocol is acceptable.

G. **What about heartworm in cats?** The infection rate of cats with heartworm is about 10% of that seen in unprotected dogs in any given area. Since close to 100% of unprotected dogs in the gulf states are infected, we can assume that up to 10% of cats being rescued from the hurricane aftermath are likely infected as well. Of those, only a fraction will experience adverse effects from their infection. Diagnosing heartworm disease in cats is problematic. Because cats generally have low worm burdens, false negatives are common with antigen based tests (the type most commonly used for screening in dogs). A positive antibody test (e.g.

Witness® FHW) indicates a history of exposure, but does not confirm current infection. Both tests used in series (screening for antibodies, followed by antigen test on cats positive for antibodies) are recommended for reasonable accuracy (Snyder et al., JAVMA March 2000). However, screening all hurricane refugee cats would be costly and may not be the best use of limited resources in the rescue effort. Unlike dogs, cats do not pose a risk of infection to other animals (they do not develop high levels of circulating microfilaria), and there is no specific treatment. For this reason, it may be appropriate NOT to test all cats, but simply to advise new owners of the possibility of infection. An informational sheet for new owners is available on our website. For more information on heartworm disease in cats, clinical signs and treatment there-of, please see the website for the American Heartworm Society at www.heartwormsociety.org

H. **Summary compromise recommendation for cats:** Don't test, DO tell. Let prospective adopters know, in a non-alarmist way, about the small risk of complications associated with heartworm infection so they can inform their own veterinarian.

[1]Much of this information comes from the *American Heartworm Society 2005 Guidelines for the Diagnosis, Prevention and Management of Heartworm (Dirofilaria immitis) Infection in Dogs*, available at http://www.heartwormsociety.org/CanineHeartwormInfo.htm

[2]Bowman *et al*. Effects of long-term administration of ivermectin and milbemycin oxime on circulating microfilariae and parasite antigenemia in dogs with patent heartworm infections. Heartworm Symposium, '92 [Trial 3 below has not been published]

Treatment of dogs with naturally acquired infections:[2] Trial 1: In 6 dogs treated with HeartGard, one dog had circulating microfilariae 301 days after the beginning of treatment. In 6 dogs receiving Interceptor, none of the dogs had circulating microfilariae after 6 months. In 6 dogs that received Interceptor for only 6 months, one dog had intermittent low levels of microfilariae in its blood throughout the study, and in one dog, microfilariae appeared again in the blood at the end of a year. In a second Trial, of 10 dogs treated with Heartgard for a year, one dog had levels that fluctuated to levels over 4,000 microfilariae per milliliter, and it was never cleared of its microfilariae. A second dog became negative after the second treatment, but recrudesced after the sixth and remained positive. Eight of the dogs became virtually negative after anywhere from 2 to 8 months of treatment, but 2 of these dogs did continue to have sporadic microfilariae detected in the blood. In a third Trial, 8 dogs with natural heartworm infections were treated with Interceptor for over six months, and three of these dogs still had circulating microfilariae.

[3] Personal communication, Brenda Griffin, DVM, ACVIM, Auburn University, Auburn, AL

[4] Additional notes on ivermectin: Be careful when calculating doses and administering ivermectin solution, as the concentration in most available solutions is very high compared to the dose needed for small animal treatment. Remember 1% solution = 1 gram/100 ml = 10 mg/ml = 10,000 ug/ml. For a microfilaricidal dose of 50 micrograms per kg for a 10 kg dog, you would need 500 micrograms, or 500/10,000 = .05 mls of 1% solution, even smaller doses for preventive level treatment (.005 mls!). For this reason, people often dilute 1% solution with 99 mls of propylene glycol, to create a solution that is 100 micrograms per ml. The preventive dose of ivermectin for a 10 kg dog then would be .5 mls, the microfilaricidal dose would be 5 mls.