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## *ACUTE & CHRONIC FELINE BRONCHIAL DISEASE & FELINE*

## *HEARTWORM DISEASE – 5 PAGES*

### Heartworm Associated Respiratory Distress Syndrome (HARD) and HWD in Feline Patients

This disease is very frustrating for the practitioner and for the feline patient. HW behaves differently in the cat than in the dog and therefore clinical presentation and treatment options are vastly different and represent notable challenges. The current testing options are limited at best. The results between tests are highly variable and somewhat unreliable due to poor test performance in some cases and general limitations due to heartworm behavior in all testing options.

It is a known fact that HW is transmitted to the feline patient when a mosquito that has fed on an infected dog feeds on the cat. It should therefore be intuitive that indoor cats should be at less risk. However, in some studies as many as 1/3 of the cats definitively diagnosed with HW based on necropsy were indoor cats. In endemic areas, all cats are at risk and should be on prevention medication. FELV, FIV infections do not appear to increase risk.

**TOP 5 KEY DIFFERENCES BETWEEN FELINE AND CANINE HEARTWORM DISEASE**

1)LARVAE AND WORMS:
In cats a much lower % of larvae survive to adulthood. The adult worms are smaller and cats have less worm burdens overall. There are higher rates of single worm or all male infections. The chances of seeing microfilaria is < 20% modified Knott or Millipore filter), and the worm survives only 2 to 3 years in the cat when compared with 5 to 7 years in the dog.

2)MIGRATION:
Cats are more likely to have HW larvae migrating to locations outside heart and lungs. The cats can remain asymptomatic or signs may be associated with local infiltration. An example of this is neurologic signs when larvae are migrating in brain.

3)ORGAN AFFECTED:

The organ most affected in cats is the lung and they can develop clinical signs during larval stages when the HW is not yet present in the heart.

4)CLINICAL SIGNS:
Clinical signs are most commonly associated with respiratory, digestive, neurologic systems as well as sudden death. Dyspnea 45%, vomiting 34%, chronic vomiting 38%, coughing 29%, sudden death 19%, neurologic signs 14%.

The clinical signs often present in two different phases. The first phase is seen during the 2-5 months while larvae are migrating and molting (late fall and early winter) and then the 2nd phase is when adult worms die and emboli in pulmonary arteries.

5)RADIOGRAPHS:
Most visible lung changes occur after 7 months post infection and EVEN transient infections can leave cats with long term lung pathology.

Pulmonary artery blunting, increased tortuosity with flattening of the diaphragm is seen less often in cats than dogs. RVE, pleural effusion, chylothorax, HM, and gallop rhythms are uncommon and should lead you to consider alternative diagnosis first

**RECOMMENDED DIAGNOSTIC WORK UP:**

1)Combination of Ag, Ab, and microfilaria tests. POS microfilaria only 100% reliable result.
2)Chest Radiographs
3)EKG is cases where suspicion is present and other results are negative
4)ECHO: Should be done to differentiate primary cardiac disease causing respiratory signs.

***TESTING: WHAT DO THE RESULTS MEAN*?**

The current state of testing options is almost as frustrating as the lack of effective treatment. Serological tests vary significantly in terms of performance. Neither AG nor AB test correctly identified all HW positive cats, so you cannot eliminate the possibility of infection based on Negative test results.

| Test | Brief Description | Result | Interpretation | Limitations |
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| **Antibody Test** | Detects antibodies produced in response to larvae. May detect infections as early as 2 | Negative | Lower index of suspicion: Absence of exposure, infection < 60 days old, or cat anergic to HW's. | Antibodies confirm infection with heartworm larvae, but do not confirm disease causality. May remain positive for an |

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| | months after exposure to male or female worms.<br>–sensitivity 32-90%<br>- specificity 98-99% | Positive | Increasing index of suspicion. Can mean current infection with larval adults, previous infection with Antibody persistence, false positive, or may have aborted infection prior to maturation into adult (ex: those cats on prevention) | unpredictable time after infection is cleared. Means infection has occurred, not necessarily current. |
| **Antigen Test** | -detects proteins from the adult **female repro tract**<br>–sensitivity 68-86%<br>- specificity 98-99% | Negative | Lowers index of suspicion. May mean no HW, infections < 7 months old, all male worms, low worm count, false negative. | Low worm counts and male-only worm infections are rarely detected. May remain POS for unpredictable amount of time after infection cleared. |
| | | Positive | Confirms presence of HW, recently cleared infection or false positive result. | |
| **Thoracic Radiography** | Detects vascular enlargement (inflammation caused by young L5 and, later, hypertrophy), pulmonary parenchymal inflammation, and edema. | Normal | Lower index of suspicion | Radiographic signs subjective and affected by clinical interpretation. Most radiographic changes occur >7 months after infection. Cats can develop clinical signs before HW reaches the heart. Severity of clinical signs does not correlate with worm burden. Transient infections can leave cats with long term lung pathology. |
| | | Signs consistent with FHD | Enlarged arteries greatly increases index of suspicion | |
| **Echocardiography** | Detects echogenic walls of the immature or mature heartworm residing in the lumen of the pulmonary arterial tree, if within the visual window of the ultrasound. | No worms seen | No change to index of suspicion | Ultrasonographer experience with heartworm detection appears to influence accuracy rate. |
| | | Worms seen | Confirms presence of heartworms in the structure | |

**THE ROLE OF WOLBACHIA**:

Research shows there is a bacterium called Wolbachia which colonizes each HW. It has substantial inflammatory effects when the HW's are dying or molting. In humans doxycycline is used prior to treatment to sterilize the HW and lead to fewer anti-inflammatory effects. The treatment of HW in cats with an adulticide or manual removal is associated with high morbidity rates and is generally contraindicated. Elimination of the Wolbachia organisms may help the cat co-exist more comfortably with its HW when they are dying or molting.

**PROGNOSIS:** Respiratory signs can often be managed with anti-inflammatory medications, bronchodilators and antibiotics. Most costs outlive their HW's but clients must be warned of the consequences such as thromboembolism, sudden death or neurologic signs.

**TREATMENT/PREVENTION**

| | |
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| **Clinical Signs: Chronic or Cyclical** | HW prevention monthly<br><br>Prednisone 1-2mg/kg PO q48-72 hours<br><br>+/- Doxycycline 5mg/kg PO |
| **Acute Respiratory Distress** | Oxygen<br><br>Dex 1mg/kg IV/IM or<br><br>Prednisilone sodium succinate 50-100mg/cat<br><br>Aminophylline 6.6 mg/kg IM q12 or<br><br>Theophylline ER 10mg/kg P.O. or<br><br>Terbutaline 0.01 mg/kg S/C<br><br>+/-Doxycycline 5mg/kg PO<br><br>HW prevention Monthly |
| **Asymptomatic Ag +ve** | HW prevention<br><br>+/- Doxycycline 5mg/kg PO |
| **Asymptomatic Ab +ve** | HW prevention<br><br>+/- Doxycycline 5mg/kg PO |
| **Asymptomatic Ag and Ab negative** | HW prevention |

**Here is some updated and additional information for your consideration:**

- *ALL* bronchial and vomiting disease in cats CAN be caused by HW ***even WHEN*** Ab test is neg, Ag test is neg, No Adult HW has ever developed, echo is normal, and bronchial changes on radiographs are not that severe!!

- Testing chronic bronchial cats for HW is likely to unrewarding even if clinical signs are induced by the immature forms because often the cats Ab status becomes negative 3 to 4 months after the original insult.

- Adults generally live for 2 to 4 years and the death of A SINGLE worm can result in ARDS (Acute Respiratory Distress Syndrome). Most cats will survive this phase if treated, as the worms tend to die slowly over time.

- Oddly enough, the existence of a single adult worm can decrease the inflammatory reaction in the lungs through suppression of monocytes. So clinical signs may be decreased and even radiographic abnormalities may be decreased.

- Lung recovery is not uniform and fragments of worms are common, so healthy lung can exist next to severely diseased lung. The lung changes are not limited to bronchial spasticity and therefore it is not truly an "asthma like" syndrome. There are bronchial, peribronchial and interstitial tissue changes.

- Testing for Ab is limited in accuracy due to highly variable lab accuracy (depending on lab and assay proteins used for different stages of larval forms), many cats will seroconvert to negative within 3 months, and even if Ab positive the HW may or may not have made it to the distal pulmonary artery as immature adults.

- Testing for Ag is also problematic given the vast majority of problems in cats are related to larval forms and the test detects Ag from **female adult** reproductive tract.

- Recent research has shown that feline asthma may be linked to mast cell degranulation in cases of feline rhinitis. The actual trigger is surmised to be anterior in the nasal cavity with secondary manifestation in the lungs (Venema ACVIM 2011).

- Reineke ACVIM 2011: In patients with pleural space disease, thoracic ultrasound can confirm auscultatory findings and differentiate between etiologies. In addition, ultrasound can help aid in performing life-saving thoracocentesis. Evaluation of left atrial size, chamber volume and contractility can help aid in the diagnosis of congestive heart failure in patients with suspected parenchymal disease. Measurements of the left atria and aortic root should be obtained by placing a line at a 45 degree angle from perpendicular which passes through the aorta and the body of the left atrium. In the normal dog and cat, the ratio of left atria to aortic root size is usually less than 1.3. Values greater than 1.5 suggest left atrial dilation and provides supportive evidence for congestive heart failure.

**Biomarker evaluation:** Drobatz ACVIM 2011: N-terminal pro-brain natriuretic peptide (NT-proBNP) and N-terminal proatrial natriuretic peptide (NT-proANP)have been evaluated for their usefulness in distinguishing heart disease from primary respiratory disease as the cause for respiratory difficulty in cats. A cutoff value of 265 pmol/L for NT-proBNP resulted in 90.2% sensitivity, 87.9% specificity, 92% positive predictive value, and 85.3% negative predictive value (area under ROC curve, 0.94) in distinguishing cats with cardiac disease compared to a primary respiratory cause of respiratory difficulty. A cutoff of 517 fmol/mL for NT-proANP concentration had a sensitivity of 90% and specificity of 82% for detecting cardiomyopathy in cats.3,4 Troponin I has also been investigated as a diagnostic tool for CHF as a cause for respiratory distress in cats. A cut-off of 0.81 ng/ml identified cardiac disease as the cause for

respiratory distress with a sensitivity and specificity of 65.2% and 90.0% respectively. However, the authors noted that there was considerable overlap in troponin concentrations between the 2 groups and therefore this modality should be used in conjunction with other evidence in evaluating for heart failure.

**So WHAT NOW**? As a clinician this is an extremely difficult situation. The best description we have heard yet was given at ACVIM this year and may be useful in discussing HW and bronchial disease in cats.

**"The juvenile delinquent form of HW is a hit and run driver in cats. The immature forms come in and create disease, and any evidence that they were the cause is not present by the time we arrive at the scene."**

#1) Remember Clinical Signs:

*dyspnea 45%, vomiting 34%,chronic vomiting 38%, coughing 29%, sudden death 19%, neurologic 19%

#2) HW prevention should be recommended for **ALL** cats in areas where it is considered prudent to have dogs on prevention.

"If Canine Heartworm is a problem in your area, it is said: You may not be seeing cats with heartworm, but they are likely seeing you."

#3) Remember Critical Time Frames for Presentation: but don't be confined by them.

a) 2.5 to 3 months after being infected by mosquito or 3 to 7 months after peak mosquito season. This is the time frame of the first arrival of larval forms at the lungs creating an intense inflammatory reaction.

b) If becomes an adult: this may suppress macrophage activity and clinical signs may be absent or intermittent and even radiographic appearance may improve.

c) Death of the mature heartworm 2 to 4 years later. Acute Respiratory Distress Syndrome can result from the death of even a single worm. This is less common than the problem with larval forms.

#4) ALL BRONCHIAL AND VOMITING Disorders can be caused by heartworm disease in cats.

#5) There is NO good way to prove or disprove your suspicion. Testing is extremely problematic in feline heartworm given the behaviour. If your are suspicious treat as if, there is no other reasonable course of action.

#6) Prevention does not eliminate the possibility of inflammatory lung disease due to dying larval forms, but will prevent adults from forming (if compliance and drug choice are sound). There will be fewer incidences of ARDS in feline patients due to death of the **adult** worms.

There are four heartworm disease preventive products approved by the FDA for use in cats: Heartgard® for Cats (ivermectin, orally) from Merial, Interceptor® (milbemycin oxime, orally) from Novartis, Revolution® (selamectin, topically) from Pfizer and Advantage Multi™ for Cats (moxidectin / imidacloprid, topically) from Bayer. The current recommendation from the AHS is **year round** protection for all cats.

**REFRENCES:**

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5)ACVIM 2011

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