



Updates in Canine Heartworm Disease

June 8th, 2023

Marisa K Ames DVM, DACVIM
Consultant to Heska



Photo: Dr. Steven Jones



Resources

- <https://www.heartwormsociety.org/>
- <https://capcvet.org/>
- <https://www.sheltervet.org/>



Macrocytic lactone (ML) preventives are highly effective:

<https://www.heartwormsociety.org/veterinary-resources>



Veterinary Education

- COVID-19 Recommendations
- AHS Bulletin
- Preventative Drug Chart ***
- Triennial Heartworm Symposia
- Exam Room Scripts
- AHS Board Speaks Out
- Videos
- Resistance Statement
- Heartworm University

Prevention

Cure



Outline

- Epidemiology
- Pathophysiology
- Prevention
- Screening & Diagnosis
- Treatment



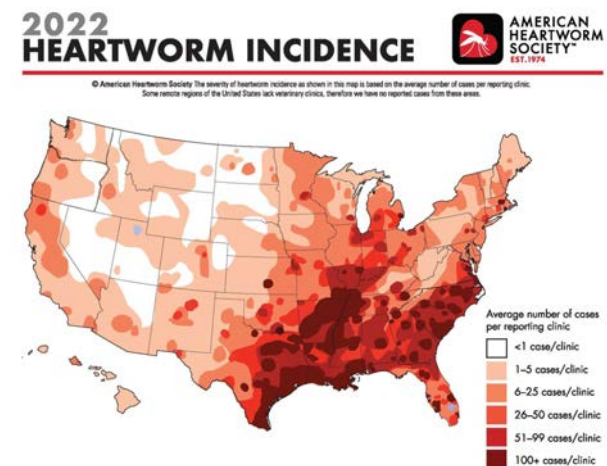
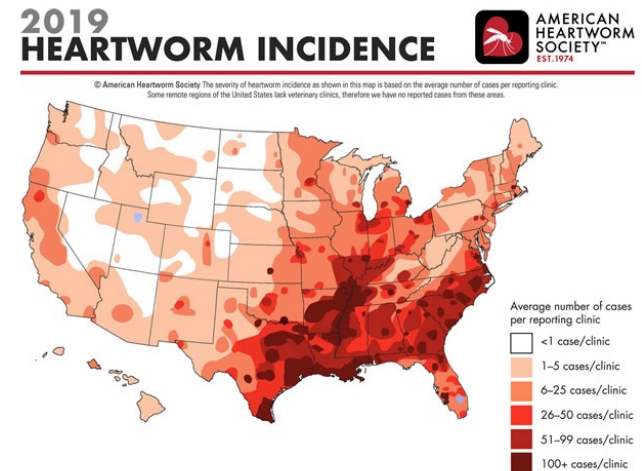
Dirofilaria immitis

- Nematode
- Transmitted by a mosquito vector
 - *Aedes*, *Culex*, *Anopheles*
 - *D. immitis* must complete L1 to L3 molts in mosquito
 - L3 is the infective stage
- Primarily affects *Canidae*
 - ALL AGES SUSCEPTIBLE TO INFECTION
- Atypical hosts: cats, ferrets, sea lions...



Incidence in the USA

- Incidence appears to be increasing
 - ~250,000 cases reported annually
 - Actual incidence is greater than this
- Infection documented in all states
 - Regionally endemic in lower 48 states & Hawaii
 - Hyperendemic regions (red/dark red)
 - Nearly all un-protected dogs are infected



Prevalence Data Are Imperfect... But here's an Estimate

Research in Veterinary Science 131 (2020) 104–116



Contents lists available at ScienceDirect

Research in Veterinary Science

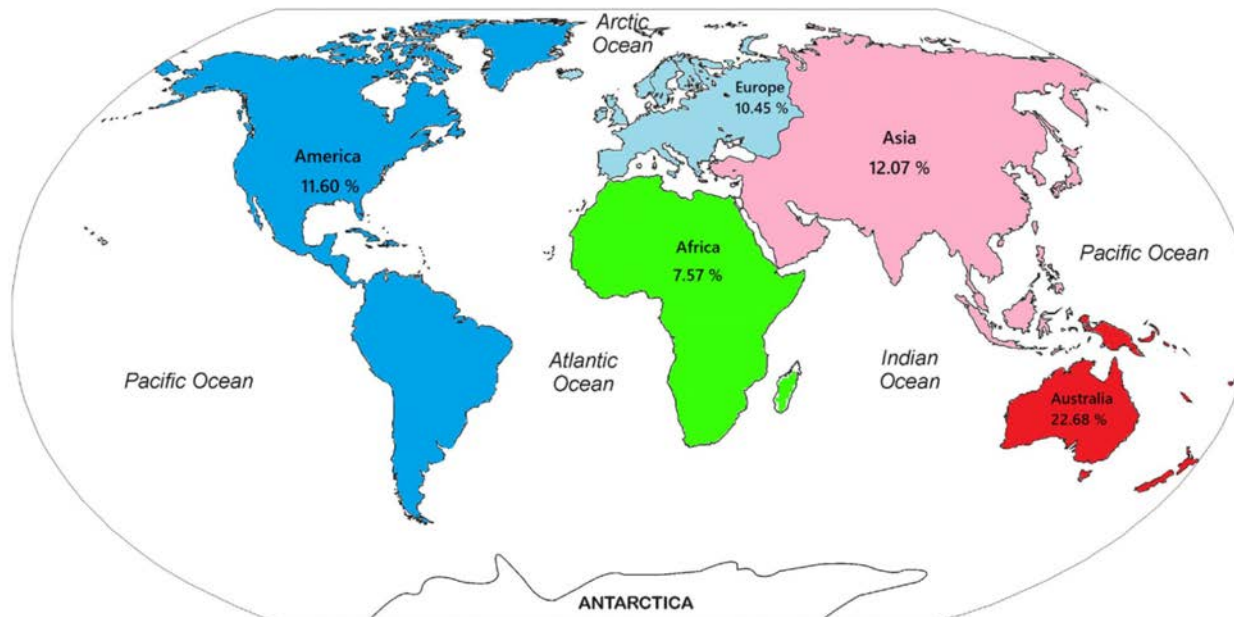
journal homepage: www.elsevier.com/locate/rvsc



The global status of *Dirofilaria immitis* in dogs: a systematic review and meta-analysis based on published articles



Davood Anvari^{a,b,c,1,*}, Elahe Narouei^d, Ahmad Daryani^b, Shahabeddin Sarvi^b, Mahmood Moosazadeh^c, Hajar Ziaei Hezarjaribi^b, Mohammad Reza Narouei^d, Shirzad Gholami^{b,1,e}



Estimated prevalence of *D. immitis* in dogs

Pooled analysis covering multiple years and various diagnostic approaches



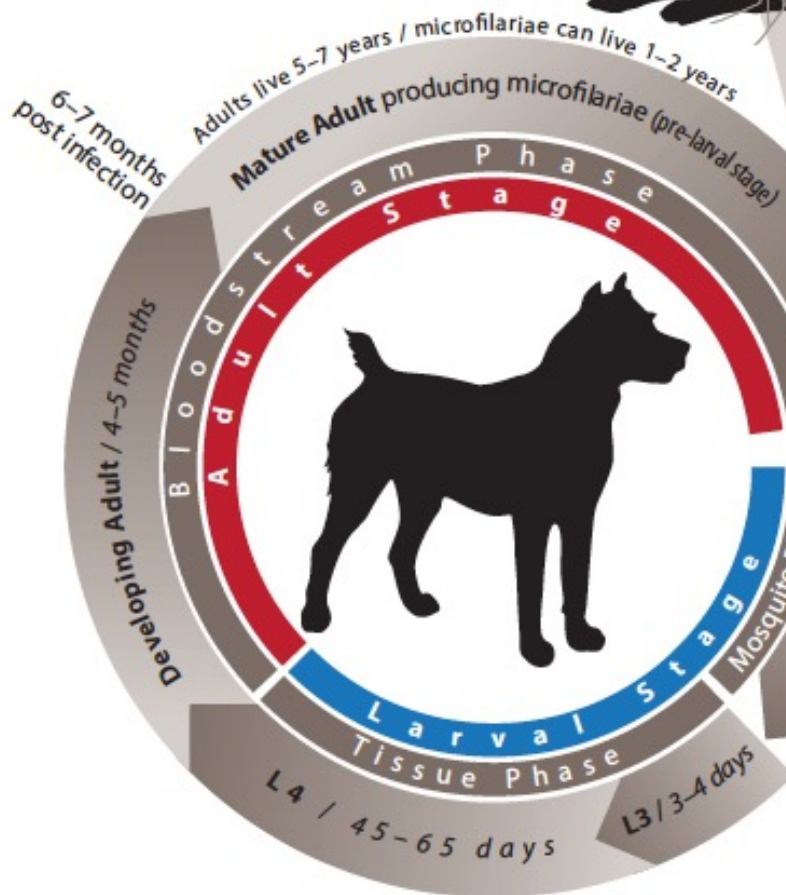
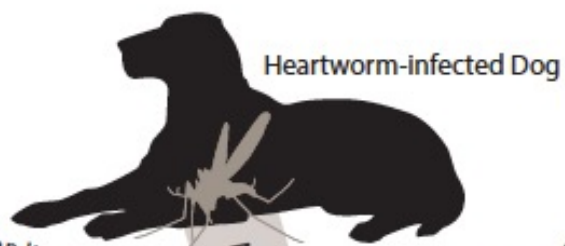
... Back to the US



Year-round transmission occurs below red line

But...this is becoming less predictable with climate change...

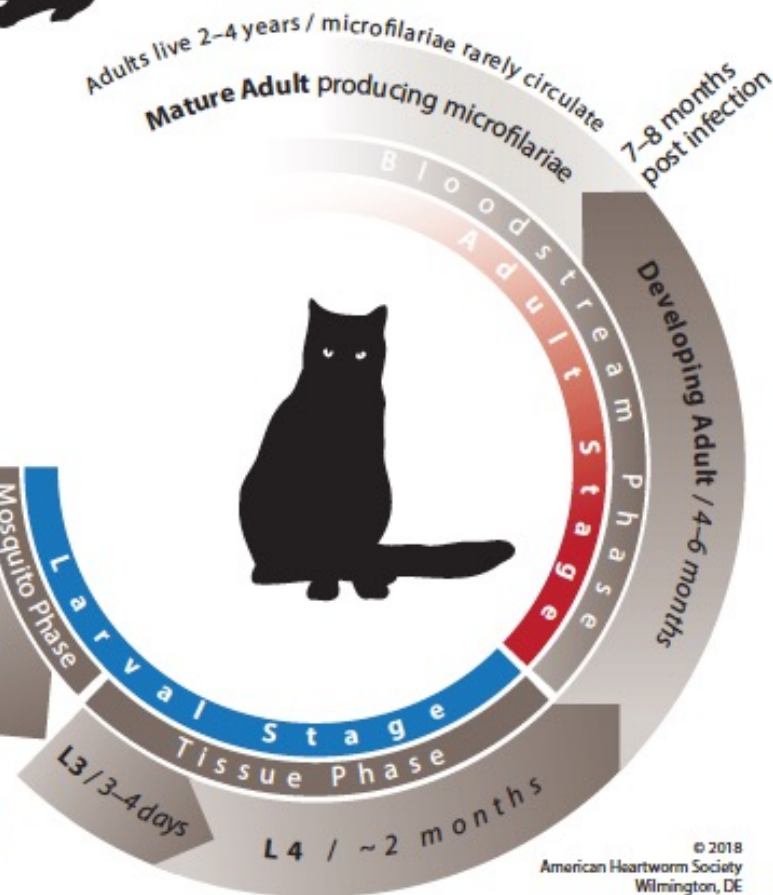
PREVENT YEAR-ROUND!



Mosquito ingests microfilariae

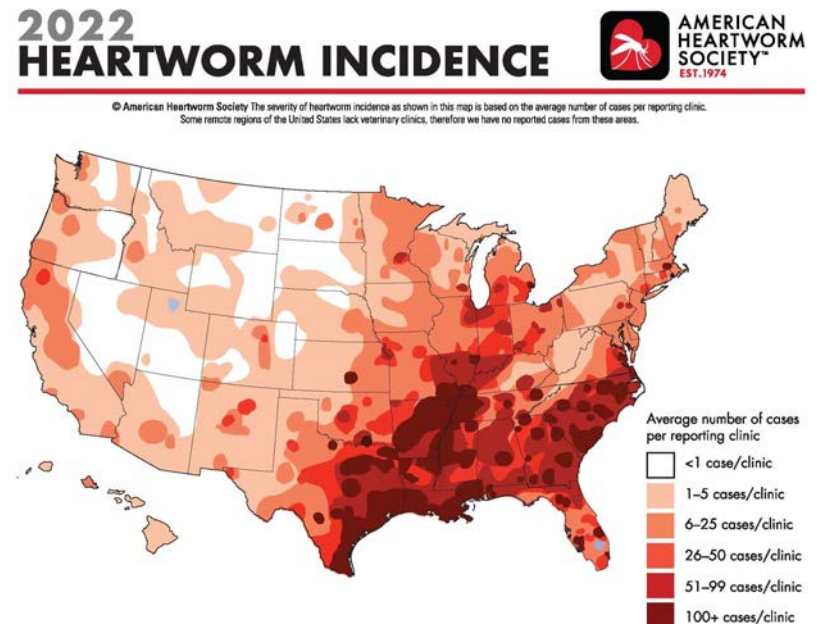
L1
v
L2
v
L3
10-14 days

Infective larvae acquire new host

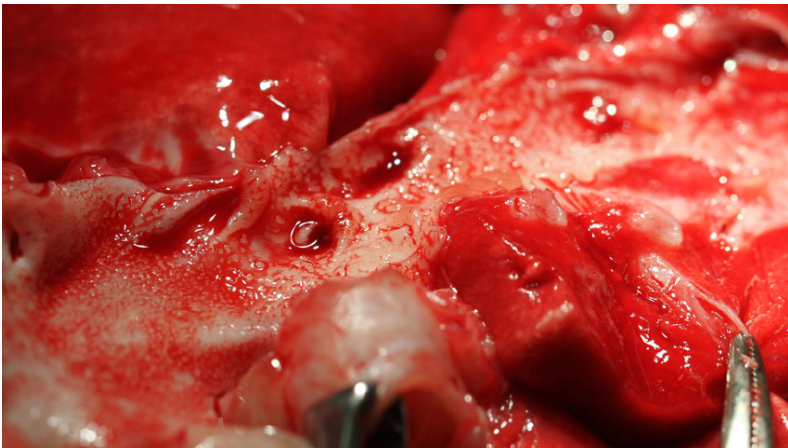
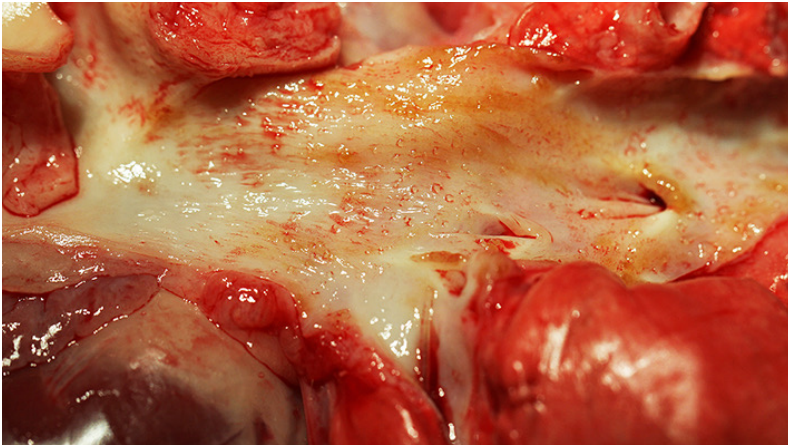


Pathophysiology

- Severity and clinical consequences:
 - Relative number of worms
 - Duration of infection
 - Host-parasite interaction
- Hard to estimate risk for complications
 - Use time exposed (age) and geography...



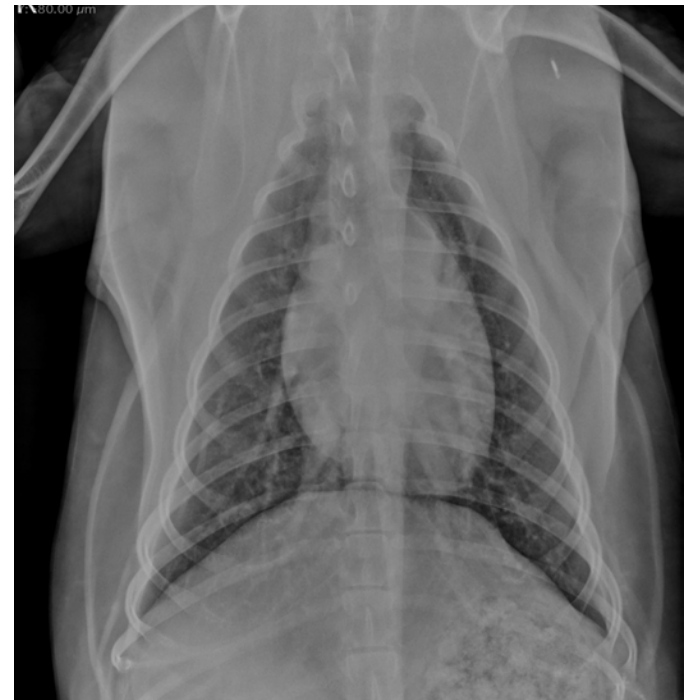
Pathophysiology



- Adult worms reside in pulmonary arteries
 - They are not usually in the heart
 - Most reside in caudal pulmonary vascular tree
 - Most worms arrive 5-7 months post-infection
- Cause pulmonary arterial damage:
 - Endothelial injury and inflammation → vasoconstriction
 - Villous arteritis and thrombosis → occlusion
 - Can lead to pulmonary hypertension in severe cases
 - Changes are partially reversible after worms eliminated

Pathophysiology

- Remarkably – most dogs have minimal clinical signs
- Cough is the most common clinical sign
 - Usually due to pneumonitis: inflammation from dying microfilaria or simply presence of worms
- Severe pulmonary hypertension may lead to right-sided heart failure
- **Test annually to catch an infection as early as possible!**

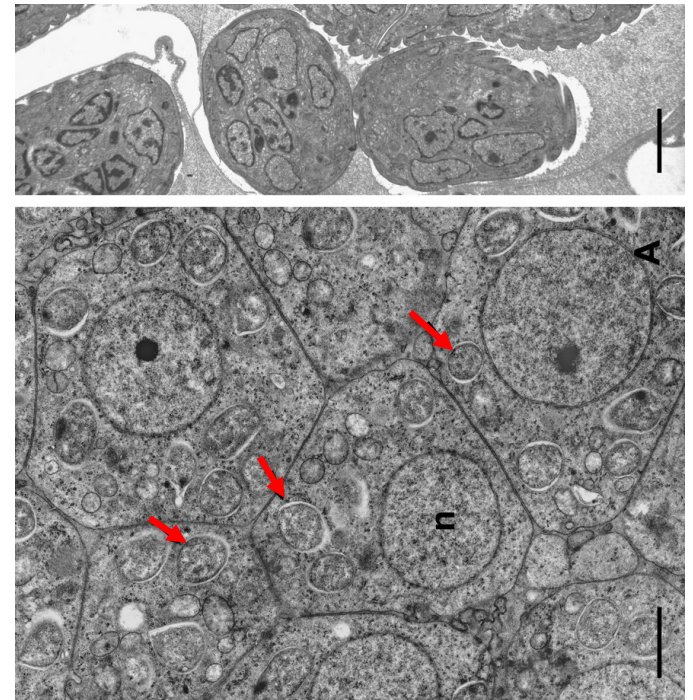


Bronchial pattern due to pneumonitis

Pathophysiology: Wolbachia

- Gram (-) intracellular bacteria
 - Ubiquitous (all life stages) and symbiotic
 - Released in large #s during release of microfilaria (Mf) and worm death → incites inflammatory response

Wolbachia (→) in *D. immitis* oocytes

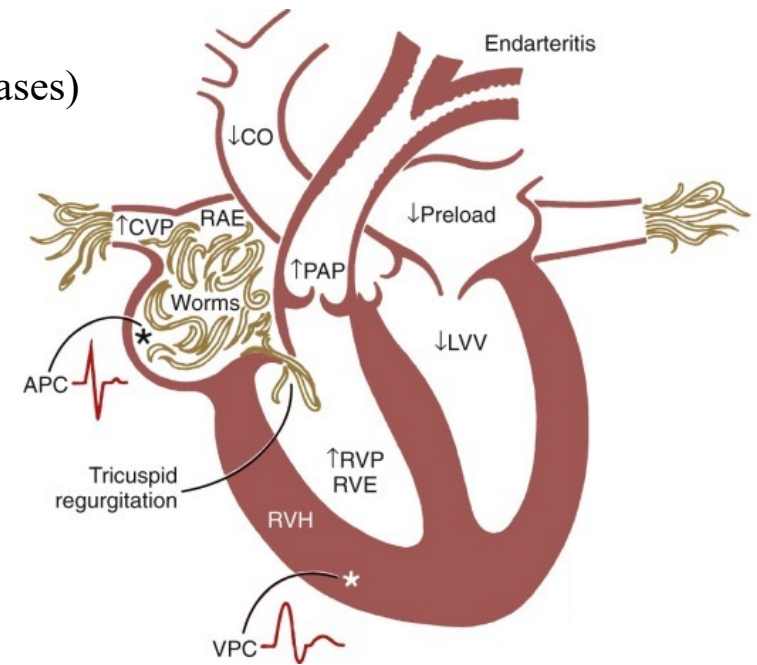


Pathophysiology: Wolbachia

- **Doxycycline** decreases # of Wolbachia in all life-stages
 - #'s remain low for 12 months after treatment
 - Renders Mf non-infective
 - Kills L3 and most L4 and weakens L5
 - Lessens pulmonary artery pathology during adulticide
 - 10mg/kg PO q12h x28d is more effective than 5mg/kg...
 - Minocycline (at same dosage) is an alternative when doxycycline unavailable

Pathophysiology: Caval Syndrome

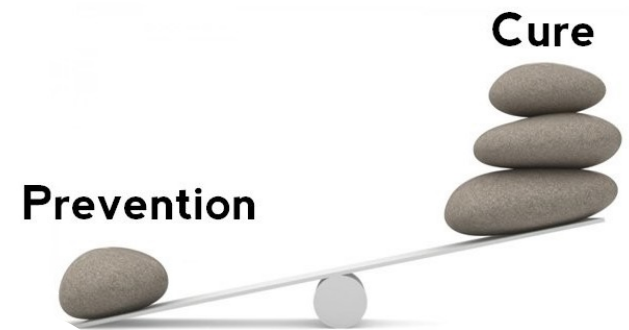
- Retrograde movement of HWs to right atrium/cavae
- Probably two situations that cause this (with overlap in certain cases)
 1. Pulmonary hypertension and R-heart dysfunction
 2. Large infection 'grows up' simultaneously → overcrowding
- Obstruction of venous return
 - **R-sided CHF, low cardiac output**
- RBCs damaged as they traverse 'sieve' of worms
 - Microangiopathic hemolytic **anemia**
 - **Pigmenturia**



Dr. Clarke Atkins

Prevention

- Heartworm preventives:
 - Macrocyclic lactone drugs: Moxidectin, ivermectin, milbemycin, selamectin
 - Kill L3 and early L4 stages with ~100% efficacy
 - ‘Reach-back’ and kill infection from past ~30 days
- Arguments for year-round prevention
 - Decreased risk of zoonotic parasitic infections
 - Collateral protection
 - Improved compliance
 - Topography, hydrography, climate varies throughout the US



Prevention

- All preventives reduce number of microfilaria
 - Moxidectin (Advantage Multi) is labeled for microfilaria clearance
 - Milbemycin is effective at clearing Mf, but is not labeled for it
 - Ivermectin will reduce circulating Mf, but 50mcg/kg needed for clearance
 - Selamectin will reduce circulating Mf, but may not clear all dogs
 - **Doxycycline levels the playing field**
 - It renders Mf non-infective after molt to L3



Screening for HW infection

- Why should you recommend yearly testing?
 - Catch an infection as early as possible
 - Surveil the efficacy of our macrocyclic lactone preventives
- Side note:
 - All preventives are safe for use in dogs with heartworm infection
 - But... hypersensitivity reactions do rarely occur
 - Also... giving heartworm infected dogs preventive could help select for resistant microfilaria

Screening and Diagnosis

- Antigen (Ag) test
 - Detects antigen found predominantly in adult female (good at detecting small female worm burdens (>3))
 - No test for all male infections
 - High sensitivity and specificity (nearly 100%)
 - False + uncommon in N. America
 - False + in Europe due to cross reaction with *Angiostrongylus vasorum* and *Dirofilaria repens*
- Microfilaria (Mf) test ideally performed with Ag test... why?
 - ID false (-) Ag test
 - If Ag+, a Mf+ result confirms infection
 - If Ag+, know Mf status prior to starting preventive



Poll (Quiz) Question

- A client admits to a 9-month lapse in administering heartworm preventative to his adult dog. How should you proceed?
 - Antigen test now and again in 12 months
 - Antigen test in 3 months and again 6 months later
 - Antigen test now and again in 6 months
 - Antigen test now and again in 3 months
- Correct answer: is antigen test now and again in 6 months



Screening and Diagnosis

- Ag detection and microfilaria appearance occurs 5-6 months post-infection
 - For practical purposes, perform antigen and microfilaria test 6 months after a ‘window of infection’
 - Because puppies are started on preventive at 6-8 weeks, their first test is at 8 months of age

Screening and Diagnosis: Results

- **Ag (+), Mf (+)**

- Diagnostic of HWI
- No need to perform 2nd Ag test to confirm

- **Ag (+), Mf (-)**

- Diagnostic of HWI
- Ideally perform 2nd Ag test to confirm
- Mf (-) result due to:
 - Macrolide preventive
 - Immune-med. destruction of Mf
 - Pre-patent infection
 - All/mostly female infection

Screening and Diagnosis: Results

- **Ag (-), Mf (+)**
 - **False negative**
 - Antigen-antibody complexing
 - Low # of female worms
 - **True negative**
 - Mf from another species (*Acanthocheilonema reconditum*)
 - Adults recently killed
 - Transplacental transmission of Mf
 - Transfusion
 - Contamination from previous sample
- Heat treatment and confirmation of Mf species can be used to sort out these scenarios




Poll (Quiz) Question

- When should heat-treatment of serum (for antigen test) be performed? Select all that apply.
 - 1. Dog has clinical signs of heartworm infection but is Ag (-)
 - 2. Dog is Ag (-) and Mf (+)
 - 3. At first antigen test 9 months following adulticide therapy
 - 4. At annual screening antigen test
- Correct answer is 1 and 2.

Clinical Signs

- Typical presentation:
 - Asymptomatic or occasional cough (most dogs)
 - Exercise intolerance
- Severe presentations:
 - Respiratory distress
 - Syncope
 - Hemoptysis
 - Abdominal distension (ascites; R-heart failure)
 - Cardiovascular collapse, pigmenturia, pallor (caval syndrome)





The Ag test is positive ...now what?

- Perform microfilaria test
- If Mf (-) confirm result with 2nd antigen test (ideally from different manufacturer)
- Additional diagnostics will depend on history/clinical signs
 - Minimum database ideal
 - Cough, tachypnea, abnormal lung sounds → chest radiographs
 - Murmur, jugular distension, effusions, syncope → echocardiogram

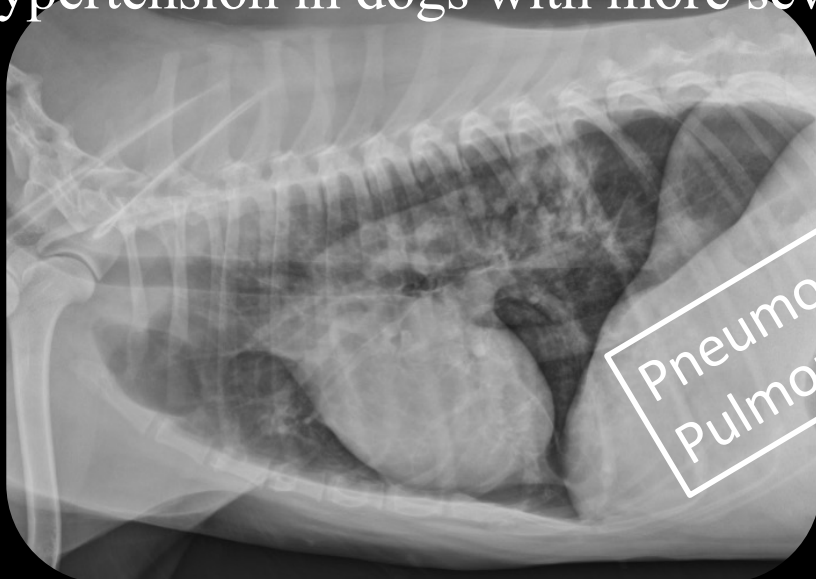
Clinical Pathology: possible - *usually mild* - findings

- CBC
 - Eosinophilia
 - Neutrophilia
 - Thrombocytopenia
 - More common 1-2 weeks post-melarsomine therapy
 - Anemia
 - Immune vs. mechanical destruction
 - Evaluate for intracardiac heartworms
- Chemistry
 - Elevation of liver enzymes
- Urinalysis
 - Proteinuria
 - Note: pigmenturia (hemoglobinuria)
 - Uncommon (and a red flag):
 - Supportive of caval syndrome → evaluate for intracardiac heartworms

Thoracic Radiographs:

Asymptomatic dogs: ideal as baseline, but not absolutely necessary...

Radiographs are indicated to investigate cough or screen for pulmonary hypertension in dogs with more severe signs



Pneumonitis &
Pulmonary Hypertension



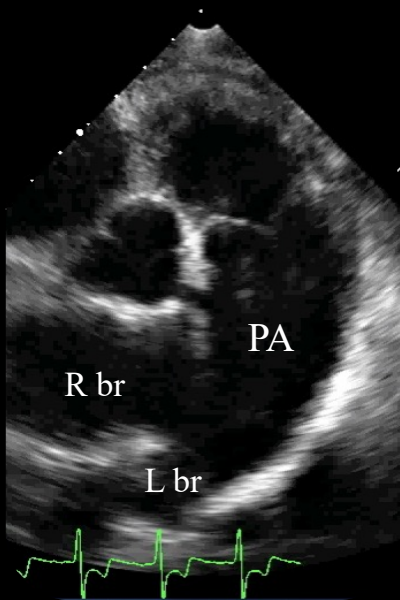
Branch pulmonary Artery Enlargement (dilated, tortuous)

Main pulmonary artery enlargement

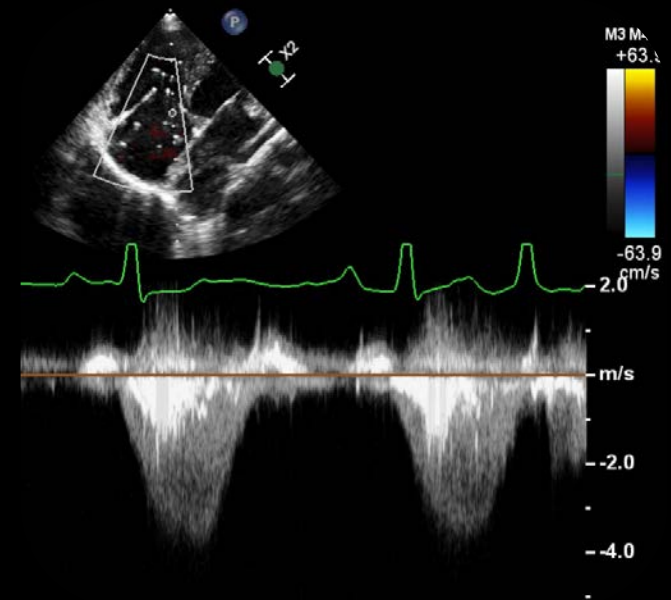
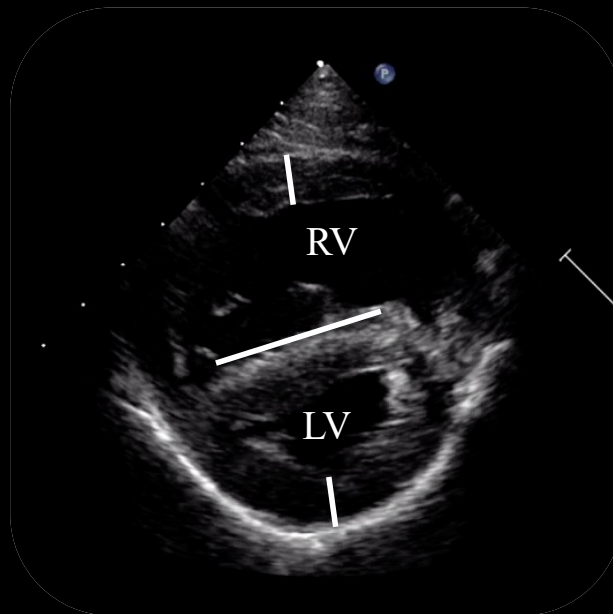
Right ventricular enlargement (reversed 'D')

Broncho-interstitial infiltrate (pneumonitis)

Echo: usually not needed. Investigate R-sided murmur or equivocal radiographic changes or clinical signs of pulmonary hypertension / R-CHF / syncope / caval syndrome



Pulmonary artery dilation
RV hypertrophy
Flattening of the IVS



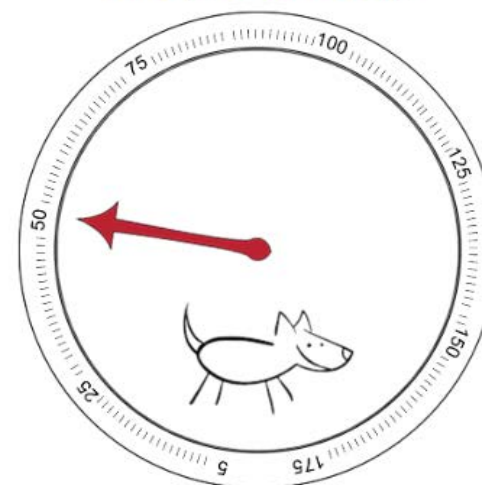
Measure tricuspid regurgitation velocity
to estimate pulmonary artery pressure

Day	Treatment
Day 0	<p>In a dog diagnosed and verified as heartworm positive:</p> <ul style="list-style-type: none"> • Positive antigen (Ag) test verified with microfilaria (MF) test • If no MF are detected, confirm with second Ag test from a different manufacturer • Apply an EPA-registered canine topical product labeled to repel and kill mosquitoes • Begin exercise restriction—the more pronounced the signs, the stricter the exercise restriction <p>If the dog is symptomatic:</p> <ul style="list-style-type: none"> • Stabilize with appropriate therapy and nursing care • Prednisone prescribed at 0.5 mg/kg BID first week, 0.5 mg/kg SID second week, 0.5 mg/kg every other day (EOD) for the third and fourth weeks
Day 1	<ul style="list-style-type: none"> • Administer appropriate heartworm preventive <ul style="list-style-type: none"> ◦ If MF are detected, pre-treat with antihistamine and glucocorticosteroids, if not already on prednisone, to reduce risk of anaphylaxis ◦ Observe for at least 8 hours for signs of reaction
Days 1–28	<ul style="list-style-type: none"> • Administer doxycycline 10 mg/kg BID for 4 weeks <ul style="list-style-type: none"> ◦ Reduces pathology associated with dead heartworms ◦ Disrupts heartworm transmission
Day 30	<ul style="list-style-type: none"> • Administer appropriate heartworm preventive • Apply an EPA-registered canine topical product to repel and kill mosquitoes
Days 31–60	A one-month wait period following doxycycline before administering melarsomine is currently recommended as it is hypothesized to allow time for the <i>Wolbachia</i> surface proteins and other metabolites to dissipate before killing the adult worms. It also allows more time for the worms to wither as they become unthrifty after the <i>Wolbachia</i> endosymbionts are eliminated.
Day 61	<ul style="list-style-type: none"> • Administer appropriate heartworm preventive • Administer first melarsomine injection, 2.5 mg/kg intramuscularly (IM) • Prescribe prednisone 0.5 mg/kg BID first week, 0.5 mg/kg SID second week, 0.5 mg/kg EOD for the third and fourth weeks • Decrease activity level even further: cage restriction; on leash when using yard
Day 90	<ul style="list-style-type: none"> • Administer appropriate heartworm preventive • Administer second melarsomine injection, 2.5 mg/kg IM • Prescribe prednisone, 0.5 mg/kg BID first week, 0.5 mg/kg SID second week, 0.5 mg/kg EOD for the third and fourth weeks
Day 91	<ul style="list-style-type: none"> • Administer third melarsomine injection, 2.5 mg/kg IM • Continue exercise restriction for 6 to 8 weeks following last melarsomine injections
Day 120	<ul style="list-style-type: none"> • Test for presence of MF <ul style="list-style-type: none"> ◦ If positive treat with a microfilaricide and retest in 4 weeks • Continue a year-round heartworm prevention program based on risk assessment described in prevention section
Day 365	<ul style="list-style-type: none"> • Antigen test 9 months after last melarsomine injection; screen for MF • If still Ag positive, re-treat with doxycycline followed by two doses of melarsomine 24 hours apart

Treatment

www.heartwormtoolkit.com

Weight of Dog



Enter Animal's Weight

50 lbs 22.7 kg

Prednisone Dose mg

11.4

Initial dose given BID and taper

Doxycycline Dose mg

227.3

Melarsomine Dose mg

56.8

Create a Treatment Plan

AHS Recommendation

- Start monthly Preventive
- Start doxycycline (10mg/kg PO q12h x 4 weeks)
- \pm Steroid taper (treat or reduce risk of pneumonitis)

- 60 and 90/91 days later:
 - Melarsomine dihydrochloride
 - Kills Adult (L5) heartworms
 - 2.5mg/kg deep IM (epaxial muscles L3-L5)
 - Strict adherence to manufacturer's instructions
 - 1 dose on day 60, then 2 doses 24h apart on day 90 and 91
 - \pm Steroid taper




AHS Recommendation

- 120 days later – ensure Mf negative
 - Most dogs will be negative
 - If still positive – consider switching to moxidectin or milbemycin product and double check that doxycycline course was appropriate
- Repeat Ag test 9 months after melarsomine
- Ensure dog is on preventive year-round for the rest of his life
- Prognosis is good for most dogs

Exercise Restriction

- Peak worm death occurs between 7-21 days post-injection
- Restrict activity during, and 6-8 weeks post melarsomine to limit:
 - Antigen release from dying worms
 - Pneumonitis, pulmonary vascular inflammation
 - Thromboembolism
 - Pulmonary hypertension

Figure 1

Phase 1 (Prior to melarsomine treatment)		Phase 2 (0-4 weeks post-injection)		Phase 3 (5-8 weeks post-injection)	
DO:	DON'T:	DO:	DON'T:	DO:	DON'T:
<ul style="list-style-type: none"> • Short leash walks • In-kennel or on-leash training • Provide in-kennel enrichment • On-leash socialization with dogs & humans 	<ul style="list-style-type: none"> • Participate in playgroups • Go for a run or long, vigorous walk • Leave unsupervised when not confined to kennel or small room 	<ul style="list-style-type: none"> • Limit walks to potty breaks only • Continue training, enrichment & socialization • Consider anxiolytics • Monitor for coughing, panting, difficulty breathing 	<ul style="list-style-type: none"> • Participate in playgroups • Leave unsupervised when not confined to kennel or small room 	<ul style="list-style-type: none"> • Slowly re-introduce leash walks • Continue training, enrichment & socialization • Allow short periods of unsupervised or unconfined activities • Monitor for signs of clinical disease 	<ul style="list-style-type: none"> • Participate in large or rowdy playgroups • Go for a run or long, vigorous walk
					

DiGangi, B: <https://www.heartwormsociety.org/veterinary-resources/veterinary-education/ahs-board-speaks-out>

What if 3-dose protocol not possible?

<https://www.shelterhwtool.com/>

Decision-Making Considerations for Heartworm Management in Shelter Dogs

Start Here

Download PDF

How to Use This Tool



If melarsomine not possible...

- **Moxidectin or Ivermectin**
 - At preventive dose every 4 weeks
 - Doxycycline 10mg/kg PO q12h x 4 weeks
 - Efficacy probably highest with topical moxidectin formulation
- Pneumonitis and heartworm thromboembolism can still occur
- Time of worm death less predictable than with melarsomine
- Exercise restriction still needed
- Recheck antigen in 9 months





Complications: Pneumonitis

- COMMON cause of cough
- Bronchial or broncho-interstitial infiltrate on radiographs
- Treatment
 - Most can be managed as an outpatient
 - If tachypnea, dyspnea
 - Oxygen
 - Steroids: dexamethasone (IV)
 - Furosemide generally not indicated / effective
 - Recommend echocardiogram to evaluate for pulmonary hypertension

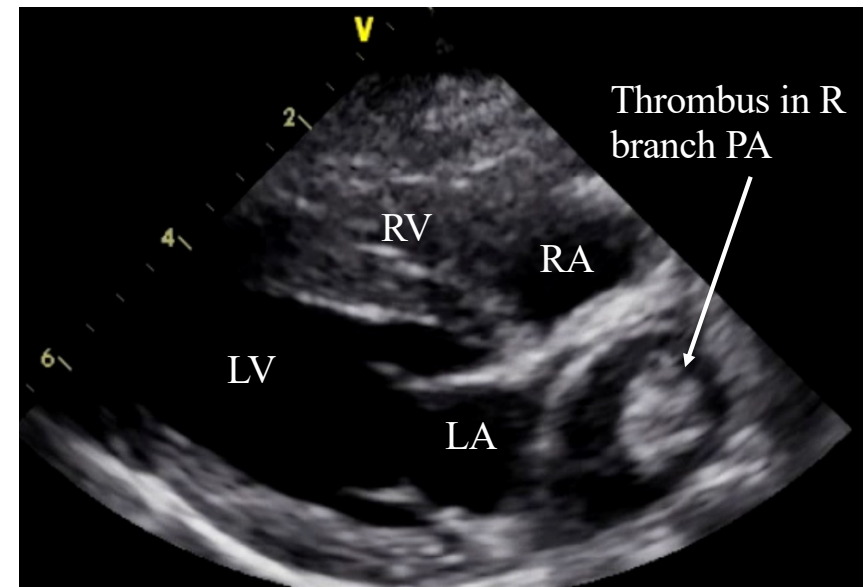


Complications: Pulmonary Hypertension

- Tachypnea, cough, syncope, cyanosis
- Radiographs
 - Radiographs usually supportive when chronic/severe
 - If radiographs normal – severe pulmonary hypertension unlikely
- Recommend echocardiogram
- Treatment: sildenafil, oxygen, rest
 - If pneumonitis present, steroids still indicated
 - If R-CHF develops:
 - Furosemide, pimobendan, spironolactone, ACE-inhibitor, and -centesis

Complications: Pulmonary Thromboembolism

- Present to some degree in all dogs that received any form of adulticide
- Probably more severe in dogs with > moderate pulmonary hypertension
- Clinical benefit from steroids appears to outweigh pro-thrombotic risk... (so use them)
- Add an anti-platelet \pm anti-coagulant?
 - Consider in cases with severe PH or visible thrombus
 - Clopidogrel
 - \pm Apixaban/Rivaroxaban



Usually not definitively diagnosed
Seeing a large, visible thrombus on echo is uncommon



Complications: Caval Syndrome

- Caval syndrome is an emergency
 - Anemia + pigmenturia + low cardiac output
 - Urgent trans-jugular HW extraction
- General anesthesia (possibly heavy sedation)
- Fluoroscopic and/or ultrasound guidance
- Usually require post-op supportive care
- If survive extraction and no complications post-operatively, prognosis fair... and can be good

Prognosis

- Ag positive dogs without clinical signs – or with mild clinical signs such as cough – tolerate adulticide well
 - Pulmonary artery damage doesn't resolve completely but improves
- Dogs with severe heartworm disease (pulmonary hypertension, right sided heart failure, caval syndrome) have a more open prognosis
 - If the pulmonary hypertension is treated and right-sided heart failure is controlled, dogs may go on to successful adulticide therapy with melarsomine
 - Caval syndrome (pigmenturia, anemia, low-output heart failure) is an emergency and usually fatal if not treated urgently

Questions?

Remember to
download the CE certificate
in the handouts panel of
the webinar control panel.

NOTE: CE certificate not available
for watching the recording.

Questions about CE?
events@heska.com

Questions about topic?
mkames@ucdavis.edu

Thank you for joining us!



©2023 Heska Corporation. All Rights Reserved. HESKA is a registered trademark of Heska Corporation in the United States and other countries. All other trademarks are the property of their respective owners.

