

Canine and feline heartworm disease – diagnosis and therapy

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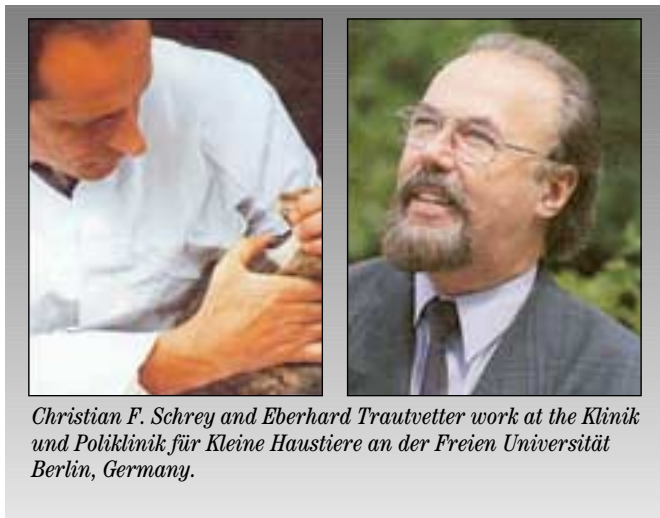


Figure 1 A diagram illustrating the global distribution of *D. immitis* infection in dogs.

KEY POINTS

- Heartworm disease is caused by a nematode worm and transmitted by mosquitoes.
- The endemic area of the disease is slowly extending.
- Dogs are the species primarily affected.
- Clinical signs vary from asymptomatic to acute dyspnea with cardiac, hepatic, and renal complications.
- Diagnosis can be difficult.
- Management of heartworm disease relies heavily on prophylaxis in endemic areas.

INTRODUCTION

Life cycle

The nematode heartworm *Dirofilaria immitis* (Leidy 1856) parasitizes the domestic dog, dingo, red wolf, red fox, coyote, ferret, sea lion, and domestic and wild cat as end hosts (1). Humans, as well as several other mammals, serve as accidental hosts in which the life cycle of *D. immitis* is not completed. Adult male (length, 12–20 cm) and female worms (length, 25–31 cm) are found primarily in the pulmonary arteries in animals with low worm burdens (< 50 worms). In infestations with high worm burdens (> 50 worms), they may be found in the right ventricle, right atrium, and occasionally in the vena cava. Pulmonary hypertension and right-sided congestive heart failure may result.

Female worms are ovoviparous and shed microfilariae (length, 220–340 μ m) into the bloodstream, where they circulate for up to 2.5 years or until they are taken up by bloodsucking culicidae (insects of

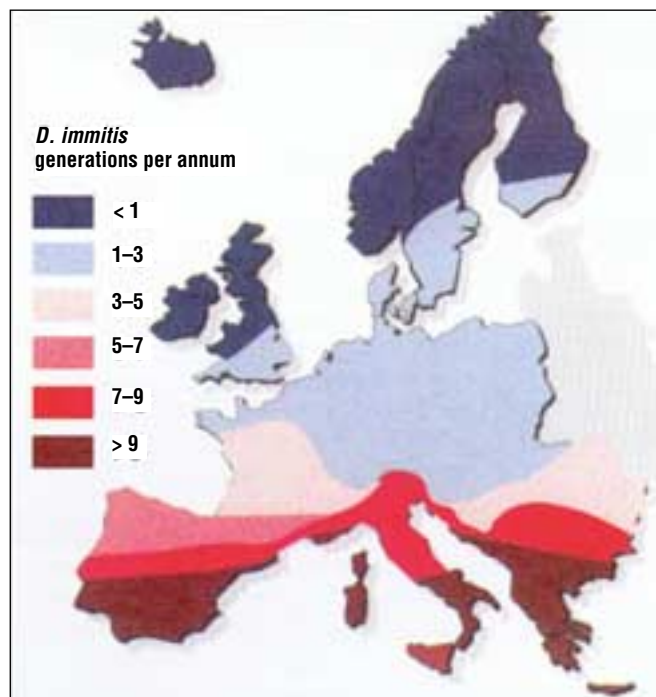


Figure 2 Climatograph of consecutive potential *D. immitis* generations in the intermediate host per year.

the mosquito family) with a blood meal. Note that microfilariae that have been transmitted transplacentally or by blood transfusion cannot develop into adult worms.

It takes approximately 2 weeks and two moults within the mosquito for microfilariae (L1) to develop into infective L3 stages. When the mosquito bites a potential host, infective L3 larvae enter the host via the insect's mouthparts. Within 70–110 days L3 stages have completed somatic migration into the host thorax, undergone two moults into L5 stages (juvenile worms), entered the vascular system via penetration of peripheral veins, and reached the pulmonary arteries, preferentially those within the caudal lung lobes.



Table 1
Clinical signs of canine heartworm disease by stage of disease

	Chronic heartworm disease			Acute heartworm disease	
	Stage I	Stage II	Stage III	Vena cava syndrome	Allergic pneumonitis
Symptoms	Asymptomatic	Exercise intolerance Sporadic cough	Lethargy Chronic, severe cough Weight loss Dyspnea Tachypnea Hemoptysis Syncope	Acute weakness Anorexia Dyspnea	Chronic, severe cough Dyspnea Anorexia Weight loss Cyanosis
Clinical signs	None	Anaemia Strong right-sided Precordial impact	Abnormal inspiratory lung sounds Anemia Peripheral venous congestion Jugular distension/pulsation Holosystolic cardiac murmur, loudest over tricuspid valve Diastolic cardiac murmur, loudest over pulmonary valve Split S2 sounds Hepatomegaly, ascites Renal failure	Hypovolemic shock Hemolytic anemia Holosystolic murmur, loudest over tricuspid valve Jugular distension/pulsation Ascites Icterus	Abnormal inspiratory lung sounds

It takes another three months of maturation (at least 190 days post-infection) before the fifth-stage larvae develop into adult worms, copulate, and produce microfilariae. The mean life expectancy of adult worms in the end host is up to 5 years in dogs and up to 2½ years in cats (2). Transplacental infections of puppies with microfilariae are known to occur (3).

Geographic distribution

D. immitis is spreading progressively from regions of subtropical climate to temperate areas. Within the last 20 years *D. immitis* has established itself in northeastern regions of the USA, parts of Canada, northern Italy, and northeastern France (4, 5). Important questions about the spreading potential of *D. immitis*, namely whether genetic or climatic adaptations of parasite and intermediate host occur, remain unanswered at present.

D. immitis is endemic in America, Africa, Asia, Australia, and southern Europe (Figure 1). Unfortunately, literature references for Asia and Africa are incomplete, as canine filarial infections have not been differentiated to species level. Imported cases of *D. immitis* infections of dogs have been reported from the United Kingdom, the Netherlands, Sweden, Hungary, Switzerland, Austria, Poland, and Germany (1). In a prevalence survey in Germany, no autochthonous *D. immitis* infections could be demonstrated, although the rate of infection in dogs with travel histories to endemic countries was high (1). Thus:

- 13% of dogs with right heart disease and travel histories to Africa, North America, Italy, Portugal, Spain, or Corsica were found to be infected with *D. immitis*.
- 10% of dogs imported into Germany from Italy, Spain, or Portugal were found to be infected with *D. immitis*.
- 12% of US Military dogs stationed in Germany were found to be infected with *D. immitis*.

Transmission

Transmission occurs by blood-sucking mosquitoes (6). The development of one generation of *D. immitis* larvae in the intermediate host is temperature dependent and occurs at a minimum of 130 HDUs (heartworm development units) (5). One HDU corresponds to 1 day with mean ambient temperatures 1°C above

14°C. At temperatures below 14°C the development of *D. immitis* larvae in the intermediate host ceases (7). Potential yearly parasite generations may be calculated (Figure 2); for example, in Heidelberg (Germany) there are potentially 4.1 generations per year:

$$4.1 = \frac{531 \text{ HDUs per year}}{130 \text{ HDUs}}$$

It is interesting to note that although heartworm disease is not endemic in Germany, the vector for heartworm disease is present and that Heidelberg (Germany) (531 HDUs/year) has similar climatic conditions to Ottawa (Canada) (513 HDUs/year), where *D. immitis* is endemic (6).

HEARTWORM DISEASE IN DOGS

Pathologic changes associated with *D. immitis* in dogs

Pathologic changes within the host system result from damage from adult worms, microfilariae, and juvenile migratory larvae. Adult worms and/or worm antigen lead to endothelial lesions, pulmonary thromboembolism, pneumonitis, pulmonary hypertension, cor pulmonale, and, ultimately, hepatic congestion, ascites, and immune-complex glomerulonephritis (Tables 1 and 2, Figure 3).

In rare cases, individual worms are wound around the tricuspid valve or *chordae tendinae* (Figure 5). When there are high worm burdens (> 50 worms), worms migrate actively from pulmonary arteries (Figure 4) into the right ventricle, right atrium, and, rarely, into the vena cava. This may lead to the acute 'vena cava syndrome', which is characterized by intravascular hemolysis, disseminated intravascular coagulation (DIC), and shock. Occasionally, ectopic infection is reported. Adult worms may be found in the anterior chamber of the eye, the skin, or the CNS. During aberrant somatic migration, juvenile larvae become trapped in these locations yet grow to adult stages. Most often they are dead upon dissection.

DIAGNOSIS OF HEARTWORM DISEASE

The diagnosis of chronic heartworm disease is based on the following:

- A history of travel to or residence in an endemic area.

Table 2
Frequency distribution of clinical signs from 47
***D. immitis*-infected dogs in Germany**

	<i>Clinical signs</i>	<i>Frequency as % (n=47)</i>
Symptoms	Asymptomatic	59.6
	Exercise intolerance	25.5
	Cough	14.9
	Dyspnea	10.6
	Syncope	2.1
Auscultation	Normal	80.9
	Systolic tricuspid murmur	10.6
	Abnormal inspiratory sounds	4.3
	Systolic pulmonary murmur	2.1
	Split-second heart sound	2.1
Radiography	Right heart enlargement	55.3
	Pulmonary vasculature changes	42.6
	Normal	38.3
	Pulmonary infiltrate	10.6
	Aortastenosis (incidental)	2.1
Electrocardiography	Normal	85.1
	Right heart enlargement	14.9
	Left heart enlargement	2.1
Laboratory	Normal	72.3
	Eosinophilia	12.8
	Thrombocytopenia	12.8
	Anemia	4.3
	Proteinuria	2.1

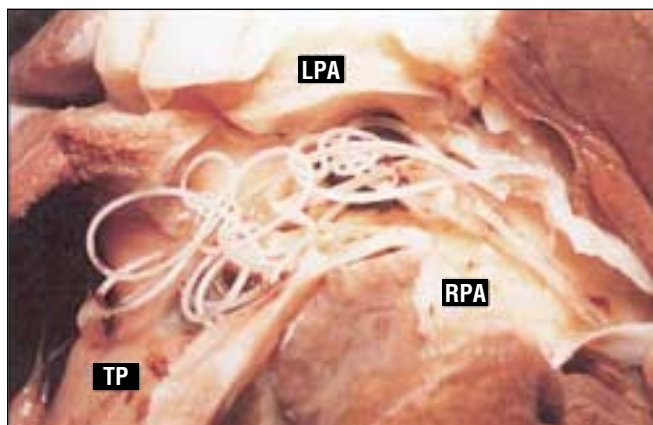


Figure 4 Adult heartworms located in the pulmonary arteries (LPA, left pulmonary artery; RPA, right pulmonary artery; TP, truncus pulmonalis).

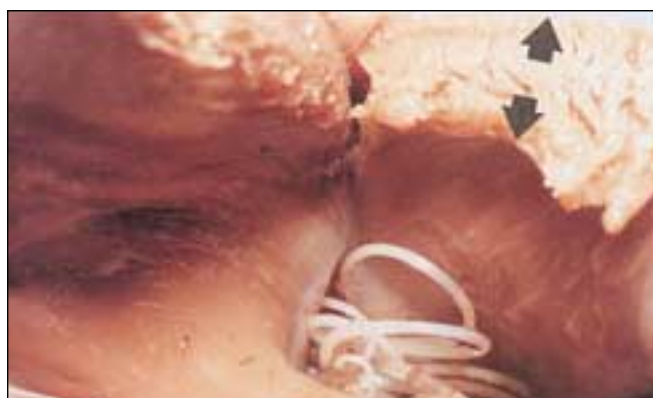


Figure 5 Adult heartworms wound around the tricuspid valve. Note the thickened walls of the ventricle (arrows).

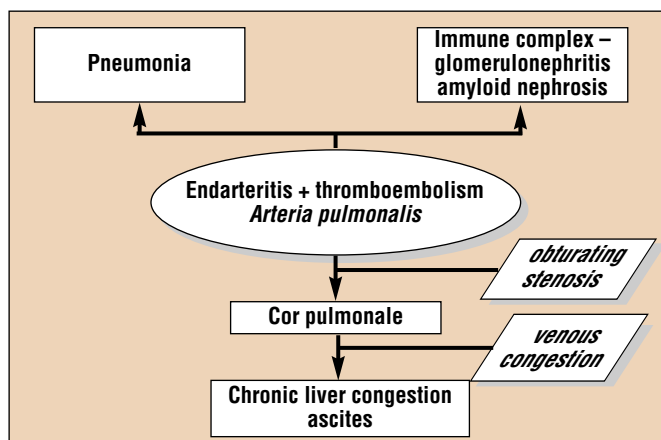
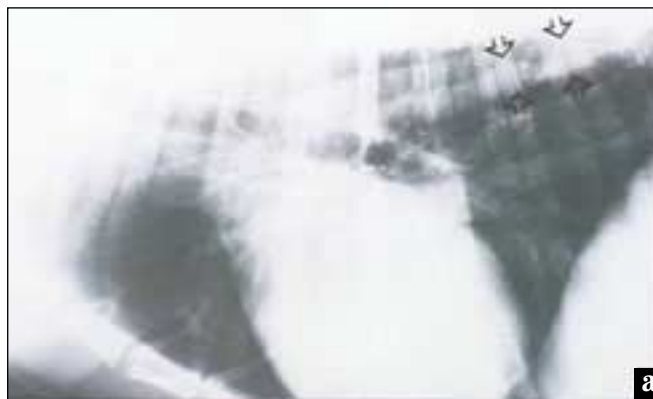


Figure 3 Schematic presentation of the pathologic changes within the host due to *D. immitis* infection.

- Clinical signs of right heart disease with typical radiographic changes (**Figure 6**) of the pulmonary arteries and supporting laboratory results (**Table 3**).
- Positive *D. immitis* microfilaria isolation test.
- Positive *D. immitis* antigen ELISA tests.

Microfilaria isolation

Reliable isolation methods for microfilariae are the Knott test and micropore filter techniques (8). When there are high numbers of microfilariae, they may be seen in direct blood smears or buffy coat smears. However, there is no correlation between microfilarial density and numbers of gravid female worms (9). Furthermore there



Figures 6 (a) and 6 (b) Lateral thoracic radiographs of two dogs with Stage III heartworm disease. **Figure 6 (a)** shows enlargement and deformation of the left pulmonary artery (arrows). **Figure 6 (b)** shows right ventricular enlargement, enlargement of the right lobar artery (arrows), and prominent perivascular densities with blunting consistent with thromboembolic disease.

Table 3

Diagnostic summary by stage of disease (Stage I is asymptomatic with no clinical signs)

Laboratory	Chronic heartworm disease			Acute heartworm disease	
	Stage I	Stage II	Stage III	Vena cava syndrome	Allergic pneumonitis
		Normocytic, normochromic anemia (PCV < 20–30%) Proteinuria (+)	Hemolytic anemia (PCV < 20%) Neutrophilia, eosinophilia, basophilia, monocytosis Thromocytopenia Hyper beta- and gamma-globulinemia Respiratory compensated metabolic acidosis Hypoxia Hypocapnia Lactate acidosis Azotemia Elevated liver enzyme concentrations Elevated creatinine concentration Proteinuria (+++)	Hemoglobinemia Hemoglobinuria Elevated liver enzyme concentrations Azotemia Stress leukogram Hyperglycemia Protein-rich abdominal effusion	Eosinophilia Basophilia Hyperglobulinemia Sterile eosinophilic tracheal exudate with neutrophils, granulocytes and macrophages
Thoracic radiography		Right ventricular cardiomegaly Enlargement of pulmonary arteries Distinct pulmonary vascular demarcation and perivascular densities – especially in the caudal lobes	Right ventricular and atrial cardiomegaly Distinct enlargement of pulmonary arteries Tortuous and deformed cranial/caudal pulmonary arteries Loss of pulmonary artery branching Patchy pulmonary interstitial or alveolar infiltrate	Hepatomegaly	Diffuse bilateral and linear pulmonary interstitial or alveolar infiltrate in the caudal lobes
Echocardiography		High worm burden: echogenic worms in the pulmonary arteries, right ventricle, and right atrium Right ventricular hypertrophy or dilatation Pericardial effusion Paradoxical septal motion Septal flattening and thickening Tricuspid valve insufficiency Elevated pulmonary artery pressure			
Electrocardiography		Sinus arrhythmia (tachycardia) Signs of right ventricular enlargement Signs of right atrial enlargement Conductive disturbances			

seems to be no seasonal or daily variation in microfilarial numbers. Thus one may examine for microfilariae at any given time. Microfilariae are able to persist in the circulation, even after adult worm death, for as long as 2.5 years. Even after perinatal infection, microfilariae are not found until a 6.5 month patency period has passed. Thus if *D. immitis* microfilariae are isolated from puppies less than 7 months old, they are acquired *in utero*.

A negative microfilaria isolation test does not rule out infection. As many as 20–30% of infected dogs harbor occult infections (infections in which adult worms are present and microfilariae cannot be demonstrated). Occult infections occur due to prepatent infections, microfilaricidal therapy, hypersensitivity reactions against microfilariae, unisexual infections, sterile adult worms, or worms in ectopic locations.

Heartworm prophylaxis with either ivermectin or milbemycin-based preparations is a common cause of occult infection in dogs

living in endemic areas. The administration of heartworm preventive medication to an infected dog will result in the gradual killing of the microfilariae within a period of approximately 6 months. The adult worms are not killed.

Upon isolation it is imperative to differentiate microfilariae to species level, since only *D. immitis* is highly pathogenic. *Dipetalonema reconditum*, *Dipetalonema dracunculoides*, and *Dipetalonema grassi* are nonpathogenic. *D. grassi* is extremely rare, and few reliable biologic data are available. *Dirofilaria repens* is only mildly pathogenic. A quick and reliable method for differentiating between microfilaria species is the acid phosphatase histochemical stain (10). Species-typical staining patterns enable the examiner to identify microfilaria species with ease (Table 4, Figures 7 and 8).

In dogs imported from Southeast Asia, sheathed microfilaria of *Brugia malayi* and *Brugia pahangi* may be found in addition to unshathed microfilariae.

Table 4

Morphologic landmarks for the typing of unsheathed, methanol-fixed microfilariae

NOTE: *D. grassi* is extremely rare and is not included

	<i>D. immitis</i>	<i>D. repens</i>	<i>D. reconditum</i>	<i>D. dracunculoides</i>
Microfilarial density	Variable	Moderate	Low	Low
Length (µm): min-max	262.1–338.2	274.6–361.9	241.2–286.9	190.8–211.8
mean ± SD	303.8 ± 18.8	308.9 ± 46.6	263.3 ± 9.9	201.4 ± 9.3
Width (µm): min-max	4–6.2	5.8–7.3	3.8–5	4.8–5.8
mean ± SD	5.5 ± 0.7	6.4 ± 0.8	4.3 ± 0.3	5.4 ± 0.5
Rostral spikes	Missing	Missing	Present	Missing
Anterior end	Conical	Right angle	Blunt	Conical
Posterior end	Straight	Straight	Often hook shaped	Straight
Motility	Local	Local	Progressive	Local

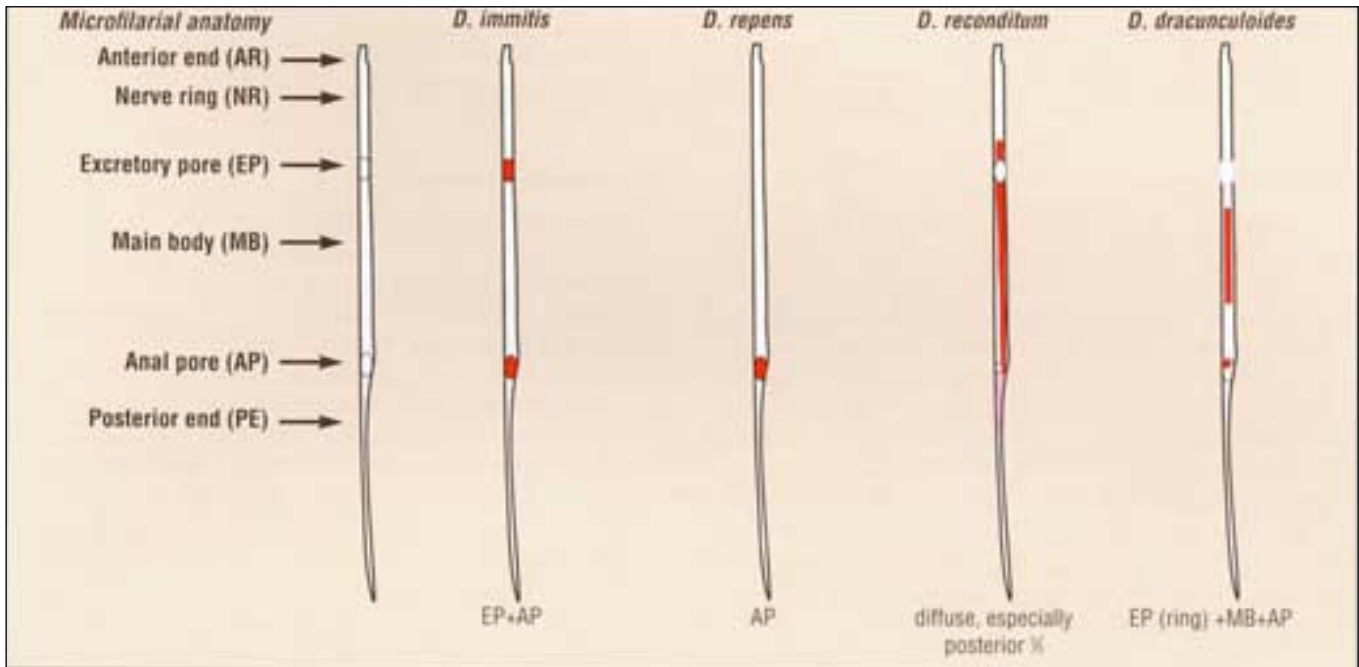


Figure 7 Acid phosphatase-staining patterns of unsheathed microfilariae (graphical presentation).

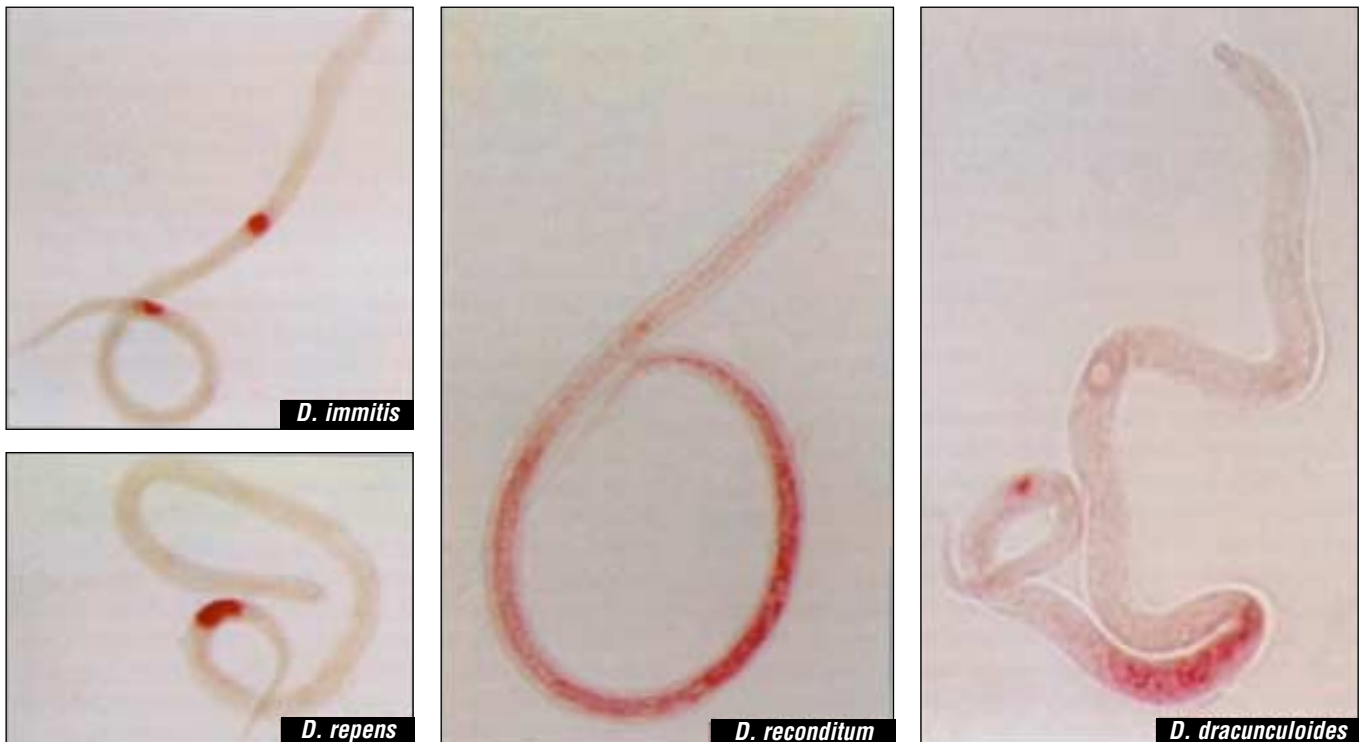


Figure 8 Acid phosphatase-staining patterns of unsheathed microfilariae (photomicrographs).

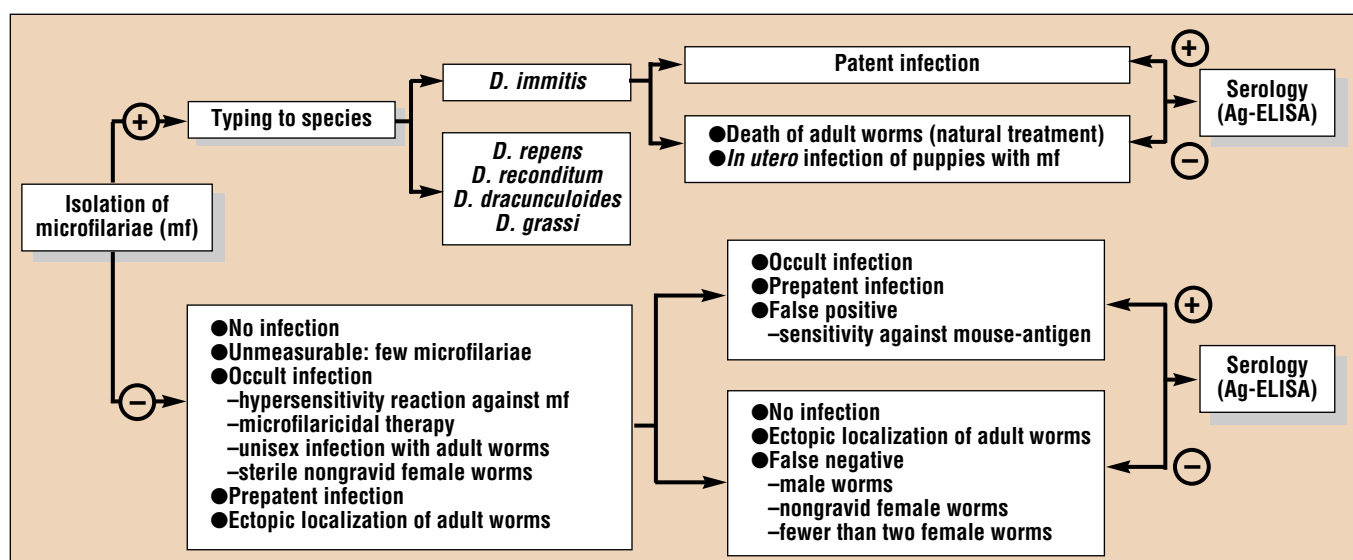


Figure 9 An algorithm illustrating the interpretation of microfilaria and Ag-ELISA test results.

Worm antigen assay

A number of *D. immitis* antigen-recognizing enzyme-linked immunoassay (ELISA) tests are commercially available. Most ELISA tests allow semiquantitative conclusions about worm burden. This is especially useful in pretreatment evaluation and treatment. In heartworm endemic areas, where prevention (using ivermectin, milbemycin, or moxidectin) is common, ELISA tests are effective in detecting occult infection. Most ELISA tests are highly sensitive and specific. However, male worms, nongravid female worms, or single worm infections are detected only with difficulty or not at all. Furthermore, some of these tests are highly sensitive to hemolytic sera while others regularly show cross-reactions with *D. repens* (1). Mouse-derived monoclonal antibodies in the test system may, on rare occasions, react with antibodies from dogs sensitized to mouse antigen, thus resulting in a false-positive test result.

In heartworm endemic areas, where there is a known prevalence of infection, the positive predictive value and negative predictive value of each ELISA test result can be calculated, thus facilitating decision-making, especially for borderline test results. In non-endemic areas a scoring system may prove useful in decision-making (1). As a differential diagnosis, lungworm infections with *Angiostrongylus vasorum* must be considered in endemic areas.

Figure 9 provides an algorithmic approach to decision-making in interpretation of microfilarial isolation and ELISA testing.

THERAPY

Many treatment strategies have been described, and they must be suited to the individual needs of each patient (Table 5).

Adulticidal therapy

The drug of choice is the trivalent arsenical, melarsamine dihydrochloride. It has proven more efficacious (efficacy, 94.2–95.7%) and is better tolerated than thiacetarsamide sodium. Melarsamine is administered intramuscularly into the lumbar musculature (11). Transient pain and local edema may follow accidental subcutaneous injection. In comparison with other adulticidal drugs, melarsamine is neither hepatotoxic nor nephrotoxic. Toxic side-effects, when they occur, commence at dosages greater than 2.5 times the recommended dose and may be antagonized by dimercaprol (at a dose of 3–5 mg/kg). Thromboembolic complications regularly occur following adulticidal therapy, especially when worm burdens are high.

Microfilaricidal therapy

Ivermectin and milbemycin oxime are highly efficient against microfilariae, third- and fourth-stage larvae, after a single administration. Although the recommended ivermectin dosage (0.05 mg/kg) is far below the critical dose for sensitive collies and bobtails (0.12 mg/kg), some authors recommend alternative microfilaricidal drugs, such as levamisol, for use in these breeds (12). Ivermectin toxic reactions in sensitive collies are poorly responsive to treatment, although one can attempt to antagonize toxicity with the administration of picrotoxin (1 mg/minute for 8 minutes) or, experimentally, with RO 15/1788 (12).

An additional complication after microfilarial therapy is anaphylactic reaction against liberated microfilarial antigen. The risk of anaphylaxis is high in small breeds of dog (< 16 kg) with high microfilarial density (> 10,000 microfilariae/ml blood). In order to prevent anaphylactic reactions, the measurement of microfilarial density before treatment and the fractioning of ivermectin portions over several days is recommended. Alternatively, heartworm prophylaxis may be started directly. Thus, microfilariae are slowly eliminated over a period of 6 months.

Supportive therapy

Platelet aggregation inhibition to prevent thromboembolic complications of adulticidal therapy can be achieved by pretreatment with either acetylsalicylic acid, acetylsalicylic acid-dipyridamol combinations, ticlopidine, or heparin. Pretreatment of dogs with Stage III heartworm disease (cardiopulmonary and thromboembolic disease) is initiated 1–2 weeks before adulticidal therapy. In some cases, pretreatment is warranted for dogs with Stage II disease (cardiopulmonary disease).

Although acetylsalicylic acid at a daily dosage of 3–5 mg/kg PO is effective in inhibiting platelet aggregation, prostaglandins E_2 and I_2 are equally inhibited. Prostaglandins E_2 and I_2 have been shown to exhibit protective functions on the integrity of pulmonary artery endothelium (13, 14). The use of acetylsalicylic acid in supportive therapy of canine heartworm disease is thus questionable. In recent years heparin administration has been recommended not only for the treatment of established thromboembolism with thrombocytopenia (150 U/kg t.i.d. SC) but also for the prevention of this complication (50–100 U/kg t.i.d. SC) (14).

Established pulmonary thromboembolism is further treated with strict cage rest, oxygen, bronchodilators, vasodilators (e.g. hydralazine), diuretics, antitussives, and broadspectrum

Table 5
Therapy guidelines of chronic canine heartworm disease

<i>Disease summary</i>	<i>Stage I</i>	<i>Stage II</i>	<i>Stage III</i>
	Asymptomatic	Cardiopulmonary disease	Cardiopulmonary disease with thromboembolic complications, liver, and renal insufficiency
<i>Prognosis</i>	Good prognosis	Fair prognosis	Guarded prognosis
<i>Therapy Goal</i>	Interrupt life cycle Eliminate adult worms as prophylactic measure	Eliminate adult worms Eliminate microfilariae	Lifesaving measures Reduce worm burden then eliminate adult worms Eliminate microfilariae
<i>Supportive treatment</i>	As a rule, none necessary	Thromboembolic prophylaxis (initiate 1–2 weeks before adulticidal therapy) Heparin Acetylsalicylic acid Acetylsalicylic acid/dipyridamol combination Ticlopidine	Thromboembolic prophylaxis Cage rest Oxygen via face mask Intravenous fluids (Glucocorticoids) Bronchodilators Vasodilators Diuretics, antibiotics
<i>Adulticidal therapy</i>	Melarsamine dihydrochloride 2.5 mg/kg twice, at 12-hour intervals or 2.2 mg/kg twice at 3-hour intervals or Thiacetarsamide sodium 2.2 mg/kg four times at 8–12 hourly intervals	Melarsamine dihydrochloride 2.5 mg/kg twice, at 12-hour intervals or 2.2 mg/kg twice at 3-hour intervals or Thiacetarsamide sodium 2.2 mg/kg four times at 8–12 hourly intervals	Melarsamine dihydrochloride 2.5 mg/kg, single dose Surgical extraction of the worms followed by adulticidal therapy when condition improves
<i>Posttreatment care</i>	At least 3 weeks cage rest	At least 3 weeks cage rest Thromboembolic prophylaxis	At least 3 weeks cage rest Thromboembolic prophylaxis
<i>Microfilaricidal therapy/ Chemoprophylaxis</i>	Microfilaricidal therapy (3–6 weeks after adulticidal therapy) • Ivermectin, 0.05 mg/kg diluted in propylene glycol 1:9 orally • Milbemycin, oxime 0.1–0.5 mg/kg orally • Levamisol, 10 mg/kg once daily for 7 days subcutaneously	Chemoprophylaxis • Ivermectin, 6–12 µg/kg once a month, orally • Milbemycin oxime, 0.5–0.9 mg/kg once a month, orally • Moxidectin, 3 µg/kg once a month, orally • (Diethylcarbamazine, 6.6 mg/kg once daily, orally)	

antibacterial agents (14, 15). Heparin administrations at 150–200 U/kg t.i.d. SC have been effective in the treatment of thrombocytopenia. Dramatic clinical improvement with life-threatening thrombocytopenias ($< 50,000/\text{mm}^3$) can be achieved with a single intravenous application of vincristine at a dosage of 0.4 mg/m².

Vena cava syndrome

The treatment of the 'vena cava syndrome' is by immediate surgical extraction of the worms occluding the vena cava and/or right atrium. After light sedation of the patient, worms are extracted by way of right jugular venotomy using flexible alligator forceps. After a recovery period of 2 weeks and thromboembolic prophylaxis with heparin or acetylsalicylic acid, regular treatment with adulticidal drugs may be initiated.

Allergic pneumonia

Allergic, or eosinophilic, pneumonia may result in response to hypersensitive reactions against microfilariae. Glucocorticoids, together with broad-spectrum antibacterial agents, should be administered until radiographic resolution of lung infiltration has been achieved. Glucocorticoids inhibit not only the killing efficacy of adulticidal drugs but also inhibit phagocytosis of dead worms. It is thus feasible to wait at least 2 weeks after glucocorticoids have been administered before starting with adulticidal drug therapy.

MONITORING THE SUCCESS OF TREATMENT

To determine the success of therapy a microfilaria isolation test should be performed 3 weeks after microfilaricidal therapy and an ELISA test 12 weeks after adulticidal therapy. If microfilariae are still present 12 weeks after adulticidal therapy and the antigen concentration is high, incomplete killing of adult worms is likely and a new course of adulticidal drugs may be started.

HEARTWORM DISEASE IN CATS

The cat is an inadequate reservoir host for *D. immitis*. Infection rates in cats are clearly lower than in dogs, even in the same endemic area. Mean worm densities are usually low with < 6 adult worms per cat. In cats, adult heartworms have a short lifespan (2–3 years) and they do not reach the same size as in dogs. The prepatent period of *D. immitis* in cats is significantly longer (8 months) than in dogs, and only approximately 50% of infected cats develop patent infections. Furthermore, patent infections are usually characterized by low microfilarial densities and self-limiting progression. After experimental transplantation of adult worms into adult cats was performed, they developed low-density microfilaraemia for 1–2 months (16, 17). Aberrant infections with ectopic location of adult worms, especially in the CNS, occur comparably frequently in cats.



Clinical signs of heartworm disease in cats

Clinical disease of cats with heartworm disease is highly variable. Sudden death following pulmonary arterial thromboembolism, severe inflammatory responses to migrating larvae, and neuropathies are not uncommon. Frequently, cats with heartworm disease present with vomiting.

Diagnosis

The diagnosis of feline heartworm disease is uncommonly difficult. Microfilariae can rarely be isolated, worm antigen often lies below measurable levels, and radiographic, as well as blood laboratory parameter, changes are subtle and nonspecific. The clinician must resort to more sensitive (and expensive) methods of diagnosis, such as echocardiography, nonselective subtraction angiography, nuclear resonance, and nuclear scintigraphy (with radiolabelled anti-*D. immitis* antibodies), in the diagnosis of feline heartworm disease. As a differential diagnosis, lungworm infections of cats with *Aelurostrongylus abstrusus* must be considered.

Therapy

Due to the short lifespan of adult worms in cats, the infections are often self-limiting. Attempts to treat infected cats with thiacetarsamide have been only moderately successful and are not recommended. In one study, toxic side-effects were reported in up to two-thirds of the treated cats (18). The use of melarsamine dihydrochloride has not been clinically evaluated for the treatment of

feline heartworm disease.

However, prophylactic monthly administration of ivermectin at 24 µg/kg PO or milbemycin oxime at 0.5 mg/kg PO is efficient to prevent infection and is well tolerated by cats.

HEARTWORM DISEASE IN HUMANS

There are several isolated reports of *D. repens* infection of humans from France, Belgium, Italy, the United Kingdom, Slovenia, Austria, and Germany. However, clinical manifestations of *D. immitis* infections of humans are rare (1). Worldwide, approximately 150 clinical cases in humans have been reported – mostly from the USA and Japan. In Europe, endemic infection and clinical disease were reported in Spain and Italy. Two cases of pulmonary *D. immitis* infections have been reported in Germany – both individuals had recently returned from Corsica (19, 20). In the province of Salamanca (Spain), *D. immitis*-specific IgM and IgG antibodies were found in 9.3% of humans examined and specific IgE antibodies in 12.6% of humans examined (21, 22).

The diagnosis of pulmonary *D. immitis* infections of humans is made by ELISA, electrophoresis, or ELISA-linked histopathologic staining of biopsy material. Chemotherapy is, as a rule, not necessary, as worms are usually dead. The surgical extraction of lung masses, where pulmonary dirofilariasis may be suspected, is a diagnostic and therapeutic necessity (19, 23).

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