

GUIDELINE for Dirofilarioses in Cats

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Synopsis

- *Dirofilaria immitis* and *Dirofilaria repens* are the most important filarial worms causing heartworm disease and subcutaneous dirofilariosis, respectively.
- The life-cycle involves an intermediate mosquito host.
- Filarial worms infect mainly dogs, but also cats, ferrets, wild carnivores and **humans**. Compared to dogs, cats are imperfect hosts to *Dirofilaria* worms. After inoculation, only a low number of L3 larvae develop to the adult stage, in a small percentage of cats.
- Heartworm disease in cats may be associated with severe pulmonary thromboembolism and eosinophilic inflammatory response in the lungs, possibly leading to sudden death. Otherwise self-cure occurs in most cases in 18-48 months.
- Subcutaneous dirofilariosis may present as subcutaneous nodules or dermatitis.
- Diagnosis in cats is more difficult compared to dogs and needs a multistep approach (antigen and antibody tests as well as diagnostic imaging).
- Cats with acute heartworm disease need intensive care unit stabilization.
- Cats with respiratory signs or suggestive radiographic changes should receive prednisolone and diagnostic follow-up should be performed. Adulticide therapy is not safe in cats.
- In endemic areas cats should be given chemoprophylaxis from 2 months of age all year long.
- *Dirofilaria repens* is currently considered an emerging zoonosis in Europe.

Agents and life cycle

Filarial worms (Spirurida, Onchocercidae) are vector-borne nematodes infecting mainly dogs but also cats, ferrets, wild carnivores (fox, jackal, coyote, wolf, raccoons, wild felids, sea lion, black bear) and humans (McCall et al., 2008; Simón et al., 2012; Otranto and Deplazes, 2019). *Dirofilaria immitis* and *Dirofilaria (Nochtiella) repens* are the most important species causing heartworm disease (HWD) and subcutaneous dirofilariosis, respectively. Both species host symbiotic bacteria of the genus *Wolbachia pipientis*, which play an important role in the biology and pathogenicity of these nematodes. These bacteria are transmitted vertically to the next generations of nematodes and are responsible for the long-term survival and reproduction of filarial worms. In fact, *W. pipientis* is involved in molting, embryogenesis and survival of filariae, and the filariae provide amino acids for *W. pipientis* bacterial growth (Simón et al., 2012).

Dirofilaria immitis adults (females 25-30 cm x ~1 mm; males 12-20 cm x 0.7-0.9 mm) reside in pulmonary arteries and right heart chambers (Figure 1) whereas those of *D. repens* (females 10-17 cm x 4-6 mm; males 5-7 cm x ~4 mm) are located in subcutaneous tissues (Figure 2) (McCall et al., 2008; Simón et al., 2012).

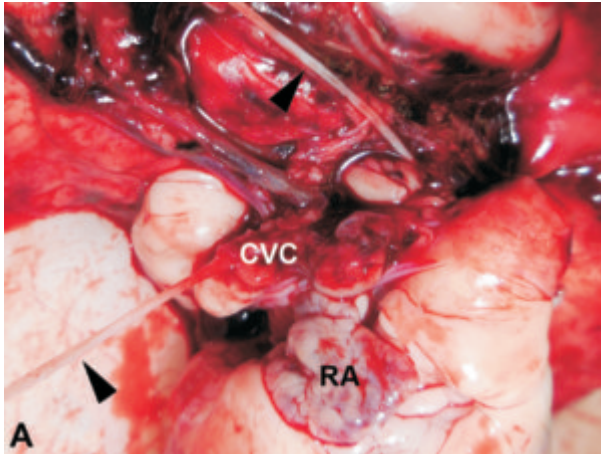


Figure 1: view of the right side of the heart of a cat affected by HWD. After removal of the pericardial sac, two adult filarial nematodes (arrowhead) were found. One of them is in the caudal vena cava (CVC). RA = right auricle. Courtesy of Ilaria Biasato and Laura Chiappino.

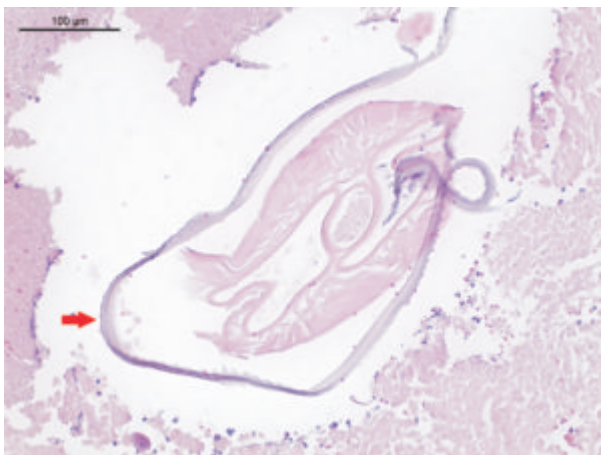


Figure 2: histological image from an adult of *D. repens* in a subcutaneous nodule on the trunk of a cat. Evenly spaced longitudinal ridges (red arrow) are visible on the surface of the cuticle. Haematoxylin and eosin. 10 X objective. Courtesy of Simone Manzocchi.

The long-lasting life cycle of these nematodes involves an intermediate mosquito host (in Europe mainly *Culex pipiens*, *Aedes vexans* and *Aedes albopictus*) that becomes infected by taking a blood meal from a reservoir host carrying an adequate number of circulating L1 larvae (microfilariae) (Cancrini et al., 2006; 2007; McCall et al., 2008; Simón et al., 2012). The most common vector species feed on humans, cats and dogs; however, the reservoir role is played by dogs or some wild canids, as cats and humans are scarcely microfilaraemic. In susceptible mosquitoes, larvae moult up to the L3 stage; these larvae are infective for the definitive hosts (Simón et al., 2012).

Cats are imperfect hosts to *Dirofilaria* worms; therefore, many important facts differ between the parasite life cycles in cats and dogs. After inoculation, only a low number of L3 larvae develop to the adult stage in a small percentage of cats, and this takes about 7-9 months for *D. immitis*. Moreover, the production of L1 larvae (microfilariae) of both *Dirofilaria* species occurs rarely (only 20% of cats with mature female and male worms) and, when microfilariae production does occur, it lasts only for a few months in feline blood and at a low load (McCall et al., 2008; Simón et al., 2012). Conversely in canine hosts about 75% filarial worms reach sexual maturity, this occurs earlier (4-6 months) and significant microfilaraemia develops and lasts for years. Finally, in cats adult worms are smaller, their life expectancy is shorter (up to 4 years) compared to dogs (over 7 years) and ectopic localizations are more frequent as a consequence of aberrant migrations of larval stages (McCall et al., 2008; Simón et al., 2012). There is only scant information about life cycle of *D. repens* in cats, however microfilariae have been found in feline hosts (Traversa et al., 2010; Simón et al., 2012; Długosz et al., 2016).

A metastrongylid nematode (*Angiostrongylus chabaudi*) is occasionally detected in the right ventricle and pulmonary arteries of European wildcats (Giannelli et al., 2016). Recently it was found in two domestic cats in Italy (Varcasia et al., 2014; Traversa et al., 2015). It is postulated that cats are occasional hosts for *A. chabaudi* because small and non-fertile parasites were detected and L1 larvae were not found in the faeces of infected cats (Giannelli et al., 2016). Moreover, pathological findings consistent with *Angiostrongylus* infection were not evident, and thus, this parasitic infection is not thought to be clinically relevant in domestic cats (Giannelli et al., 2016). The life cycle of *Angiostrongylus vasorum*, the metastrongylid species affecting dogs and wild canids, involves slugs and snails, and infection occurs by oral ingestion of infected molluscs carrying infectious L3 larvae but the intermediate host of *A. chabaudi* is still not known (Giannelli et al., 2016).

Epidemiology

Dirofilaria immitis is worldwide distributed in tropical and temperate regions and endemic in some countries in Europe and North and South America. Conversely, *D. repens* is frequently reported from Europe and Asia, infrequently from Africa and has not been found in the Americas, Australia and Japan (Yilmaz et al., 2019). In Europe, endemic areas of both species exist in Mediterranean countries (Italy, Spain, France, Greece, and Turkey) but recent extension within these countries as well as to Central and Eastern Europe (Switzerland, Austria, Germany, the Netherlands, Croatia, Serbia, Hungary, Czech Republic, Poland, and Russia) was documented (Traversa et al., 2010; Genchi et al., 2011; Mórchon et al., 2012). This spread is particularly concerning with *D. repens* as this is currently considered an emerging zoonosis in Europe (Capelli et al., 2018). Increasing mosquito abundance and seasonal activity as well as increased travelling of infected dogs are causing the spread of filarial infection. Global rising of temperatures also lengthens the seasonal timeframe adequate for maturation of larvae in the infected mosquitoes up to throughout the year (Simón et al., 2014). However, climatic differences concerning humidity also impact on the risk of exposure for susceptible hosts, particularly when the canine population is not undergoing massive chemoprophylactic treatment (Montoya-Alonso et al., 2016). According to predictive models developed for dirofilariosis, summer temperatures in Europe are able to support the life cycle of larvae in mosquitoes even in colder regions, such as UK, in case of the presence of infected reservoirs (Genchi et al., 2005; 2009; 2011). Thus far, Estonia is the northernmost European area where *D. repens* life-cycle has been demonstrated, and a human case was diagnosed even in Finland (Capelli et al., 2018).

The true prevalence of feline HWD is difficult to evaluate because of diagnostic difficulties, but infection is detected in the same areas as canine HWD at about 9-18% of the rate in unprotected dogs (Venco et al., 2011a). However, studies investigating anti-*D. immitis* antibodies in cats show that the rate of exposure to infection is much higher (Venco et al., 2011a; Montoya-Alonso et al., 2011, 2016; Diakou et al., 2019). Outdoor cats have a 3-fold higher risk of being antigen-positive and male cats are more likely to develop mature infections in experimental studies (Levy et al., 2017).

Information about the prevalence of *D. repens* infection in cats in Europe is very limited, however a study performed in central Italy using both modified Knott and PCR tests found a prevalence of 1.6% in cats compared to 5.6% in dogs. In central Poland, a prevalence rate of 0.7% in cats compared to 38% in dogs was determined by PCR (Traversa et al., 2010; Bajer et al., 2016).

Pathogenesis and clinical signs

Heartworm Disease

Despite the low parasite load (1-6 adult worms per cat), severe pathological changes are found early in cats and they can be life-threatening. Pulmonary endo-mesoarteritis with occlusive medial hypertrophy are observed as soon as immature worms arrive in the pulmonary vessels (about 3 months post-infection [p.i.]) (Dillon et al., 2007; 2014). Early death (3-4 months p.i.) of juvenile heartworms usually occurs soon after they arrive in the pulmonary arteries, otherwise they survive about 2-4 years followed by self-cure in most cases (Venco et al., 2008). Early or end-stage parasite death can be associated with acute severe lesions (severe pulmonary thromboembolism and eosinophilic inflammatory response in lungs) causing the so-called heartworm-associated respiratory disease (HARD) characterized by acute onset of dyspnoea and interstitial pattern on lung radiography (Dillon et al., 2007; García-Guasch et al., 2013; Dillon et al., 2014). In experimental studies, the inflammatory response due to the death of immature adult heartworms is associated with chronic myofibrocyte proliferation histologically evident in lungs up to 18 months after infection (Dillon et al., 2017).

Pulmonary arterial disease is associated with exposure to *D. immitis* and is considered more severe compared to dogs due to the increased activity of pulmonary intravascular macrophages in cats (Browne et al., 2005; Dillon et al., 2008). In one case, pathological changes of the arterial wall caused fatal artery dissection of the pulmonary artery (Figures 3-5) (Biasato et al., 2017).

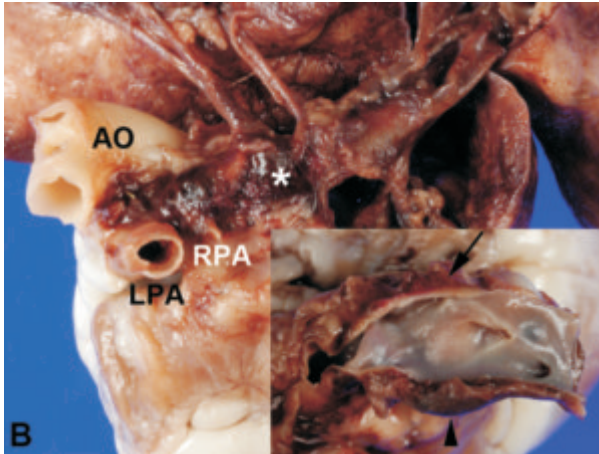


Figure 3: dorsolateral view of the pulmonary artery. Right pulmonary artery (RPA) is diffusely red and tan in colour and severely dilated (*). Upon opening (picture in the lower right), the wall of the right pulmonary artery is split with haemorrhage (arrowhead) dissecting into the tunica media. Large and multifocal peri-adventitial haematomas (arrow) are also observed. AO = aorta; LPA = left pulmonary artery. Courtesy of Ilaria Biasato and Laura Chiappino.

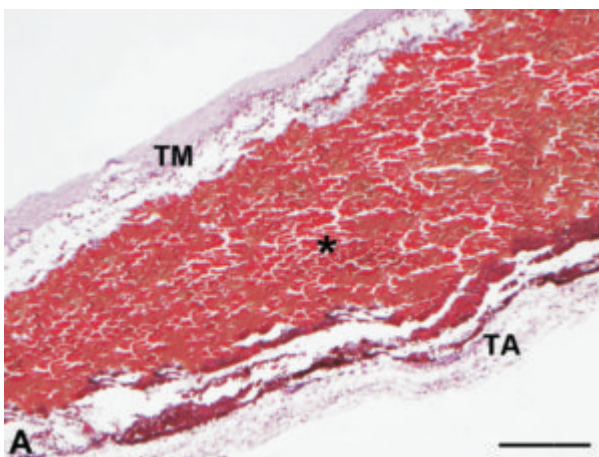


Figure 4: histopathological examination of pulmonary artery. The tunica media (TM) of the right pulmonary artery is dissected (*) by haemorrhage (Haematoxylin & Eosin stain, 2.5x magnification, bar = 1000 µm). TA = tunica adventitia. Courtesy of Ilaria Biasato and Laura Chiappino.

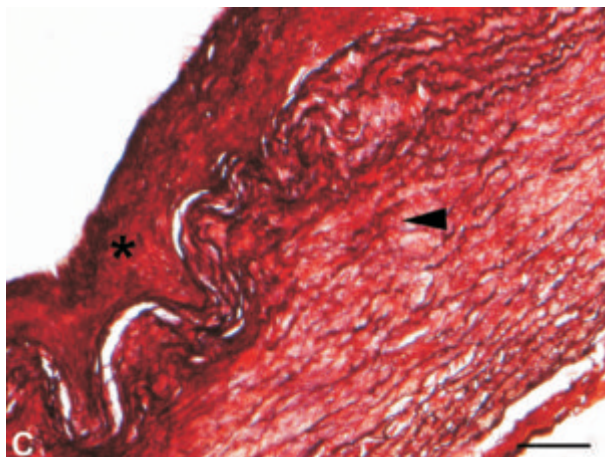


Figure 5: histopathological examination of pulmonary artery. Marked and multifocal fibrosis (*) of the tunica intima with disorganization/fragmentation of the elastic fibers and fibrous tissue deposition (arrowhead) is observed in the right pulmonary artery (Elastic Red Picro Sirius stain, 10x magnification, bar = 100 µm). Courtesy of Ilaria Biasato and Laura Chiappino.

Moreover, the presence of circulating *W. pipientis* antigens and anti-*W. pipientis* antibodies have been associated in experimentally infected cats with an inflammatory reaction in the host tissues that affect respiratory function (Mórchon et al., 2004; García-Guasch et al., 2013).

Sometimes sudden death is reported in apparently healthy cats as a consequence of severe pulmonary thromboembolic or haemorrhagic pathology, including haemothorax due to pulmonary artery dissection (Alho et al., 2016; Biasato et al., 2017; Diakou et al., 2019). According to experimental studies, an acute systemic anaphylaxis could be involved in this hyperacute course of feline HWD secondary to the release of large quantities of *D. immitis* antigens from dead parasites. The usual clinical signs are severe respiratory insufficiency, hypotension, vomiting and diarrhoea (Lister and Atwell, 2006; Lister et al., 2007). Most cats have, however, a less severe, transient and chronic course of HWD with mild to moderate respiratory signs, due to chronic bronchoalveolar inflammation (epithelial infiltration and proliferation of smooth muscle cells in bronchioles), persisting even after the parasite death. Various further clinical manifestations, such as chronic vomiting, anorexia, and cachexia, are also reported and can be the most evident clinical signs (Dillon et al., 2000). Caval syndrome is rarely observed in cats but can arise when 1-2 worms are located in the right side of the heart causing tricuspid regurgitation (Figure 1).

Aberrant migrations (e.g. in body cavities, central nervous system, femoral artery) are rare but more frequently reported in cats than in dogs and are responsible for effusions or neurological manifestations (e.g., blindness, ataxia, paraparesis, monoparesis, seizures) (McCall et al., 2008; Simón et al., 2012; Favole et al., 2013; Oldach et al., 2018). Acute-onset pelvic limb monoparesis due to femoral thromboembolism was caused in a cat by an adult 13 cm female HW extending from caudal abdominal aorta into the right external iliac and femoral arteries (Oldach et al., 2018). Interestingly, HWD had been diagnosed in this cat three years before when it was evaluated for cough and successfully treated with prednisone (Oldach et al., 2018).

Laboratory diagnosis may reveal eosinophilia on complete blood count and on bronchoalveolar lavage cytology. Changed concentrations of acute phase proteins have been described (Dillon et al., 2014; Venco et al., 2015; Silvestre-Ferreira et al., 2016). Hyperglobulinaemia, hypoalbuminaemia and proteinuria can occur in cats with HWD irrespective of their parasite burden (Atkins et al., 2011).

Subcutaneous *Dirofilariosis*

Dirofilaria repens infection is often subclinical in infected hosts; however, subcutaneous nodules or dermatitis are associated with the presence of adult worms in dogs (Venco et al., 2011b). An adult parasite or some microfilariae were incidentally found, respectively, in the subcutaneous tissue of an asymptomatic cat during elective surgery and in the blood of a stray queen and in some of her 8-week old kittens (Mazurkevich et al., 2004; Długosz et al., 2016).

Microfilaraemia or positive *D. repens*-specific PCR were found in cats with papular and crusting dermatitis (Tarello, 2011). Recently, *D. repens* adult worms were detected in a cat that was presented with 3 large (around 2 x 2 cm) firm and infiltrating subcutaneous nodules on the lateral thoracic wall and forelegs associated with axillary and inguinal lymphadenopathy (Figures 6, 7) (Manzocchi et al., 2017).

Moderate absolute eosinophilia was the only clinicopathological abnormality found and eosinophilic lymphadenitis (Figure 8) was detected on cytological evaluation of the enlarged lymph nodes (Manzocchi et al., 2017).



*Figure 6: subcutaneous nodule in the foreleg of a cat caused by *D. repens*. Courtesy of Simone Manzocchi.*



*Figure 7: subcutaneous nodule in the trunk of a cat caused by *D. repens*. Courtesy of Simone Manzocchi.*

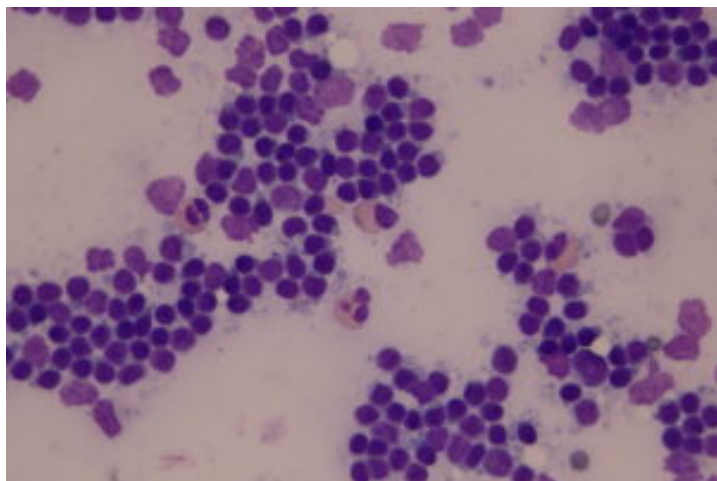


Figure 8: fine needle aspiration of axillary lymph node of a cat with subcutaneous dirofilariosis. Eosinophilic lymphadenitis. May Grünwald-Giemsa. 40 X objective. Courtesy of Simone Manzocchi.

Diagnosis

The rare and short-term occurrence of microfilaraemia and the low number of adult worms make it difficult to diagnose HWD in cats, compared to dogs. A multistep approach, combining mainly antigen and antibody tests and diagnostic imaging, is required to overcome the limitations of each single diagnostic technique (Jones et al., 2014) (Figure 9). Moreover, HARD can already occur during early death of parasites and this explains the possibility of discordant results between different tests even in symptomatic cats.

Diagnostic approach to feline HWD

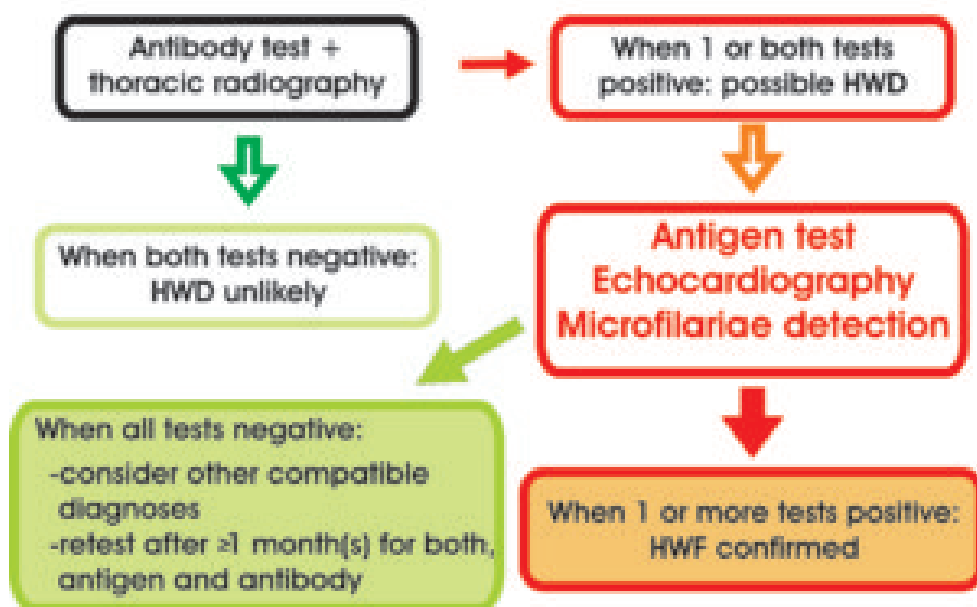


Figure 9: the combined use of different diagnostic tools is usually required to reach diagnosis of feline HWD and in some cases confirmation is never obtained. Anti-*D. immitis* antibody detection and thoracic radiography for detecting compatible pulmonary lesions are sensitive methods to have early information about possible feline HWD. However limitations of antibody detection are due to lower sensitivity in asymptomatic cats as time passed, and to antibody persistence for some time in cats that self-cure. A positive antigen test or the ultrasound visualization of filarial worms are confirmatory but their sensitivity is inadequate for excluding HWD in case of no antigen and worm detection. Rarely microfilariae are evidenced in blood (Knott test or millipore filter), but they have to be differentiated from those of *D. repens* in countries where both species are found (e.g. in Europe).

In contrast to dogs, both microscopical detection of microfilariae and ELISA or immunochromatographic (IC)-based tests that detect circulating antigens of adult *D. immitis* females have low sensitivity in cats (McCall et al., 2008; Simón et al., 2012; Jones et al., 2014; Venco et al., 2015). Albeit rarely, microfilariae of both species can incidentally be detected on feline routine blood smears and further investigations are always required for their identification (Długosz et al., 2016). When microfilariae are detected using routine techniques (modified Knott test or millipore filtration), morphometric identification, cytochemical stain or PCR are needed to differentiate *D. immitis* and *D. repens* microfilariae in countries where both species are found (e.g. in Europe) (Venco et al., 2015).

Feline HWD is usually associated with the presence of few pre-adult or adult worms. When no or only one adult female worm is present, a false negative result is obtained on ELISA or IC antigen tests (Berdoulay et al., 2004). However, heat pre-treatment of feline and canine serum or plasma samples improves the sensitivity of these commercial antigen assays in cats (and dogs) carrying only few adult female worms by releasing antigens blocked within circulating immune-complexes (Little et al., 2014; Velasquez et al., 2014; Gruntmeir et al., 2016; Little et al., 2018). In order to underline the low negative predictive value of antigen assays in cats it is suggested to record any negative result as “no antigen detected” instead of “negative” (Jones et al., 2014).

Anti-*D. immitis* antibodies are found about 2 months p.i. and they confirm exposure to *D. immitis* early irrespective of the parasite load (Prieto et al., 2002). However, a risk of false positive results exists because of antibody persistence even in cats that have cleared the parasites (Berdoulay et al., 2004). False negative results are also possible (particularly in asymptomatic cats), and a wide range of sensitivities exist among the different tests (Jones et al., 2014). The combined use of antigen and antibody testing increases diagnostic accuracy of testing for feline HWD but negative results on both tests still cannot exclude a diagnosis in suspected HARD cases.

Thoracic radiography is always indicated for the diagnosis of HWD because of suggestive changes and for prognostic reasons (Venco et al., 2015). Suggestive abnormalities include a vascular pattern (enlargement, loss of tapering, tortuosity, and truncation of the right or both caudal pulmonary arteries on ventro-dorsal thoracic radiography) and patchy infiltrates around the caudal lobar arteries resulting from plasma leakage and perivascular inflammation (often peripheral in caudal lobes) (Figure 10) or a diffuse broncho-interstitial pattern (Venco et al., 2015). Radiographic changes can be the only detected abnormality in suspected HARD cases, but lungworm disease should be excluded in these cats as a differential diagnosis for the radiographic changes (Pennisi et al., 2015). Pulmonary thromboembolism, arterial changes and bronchial collapse are common findings when cats with HWD undergo computed tomography (CT) or angiography investigations of the thorax (Dillon et al., 2014; Panopoulos et al., 2018).

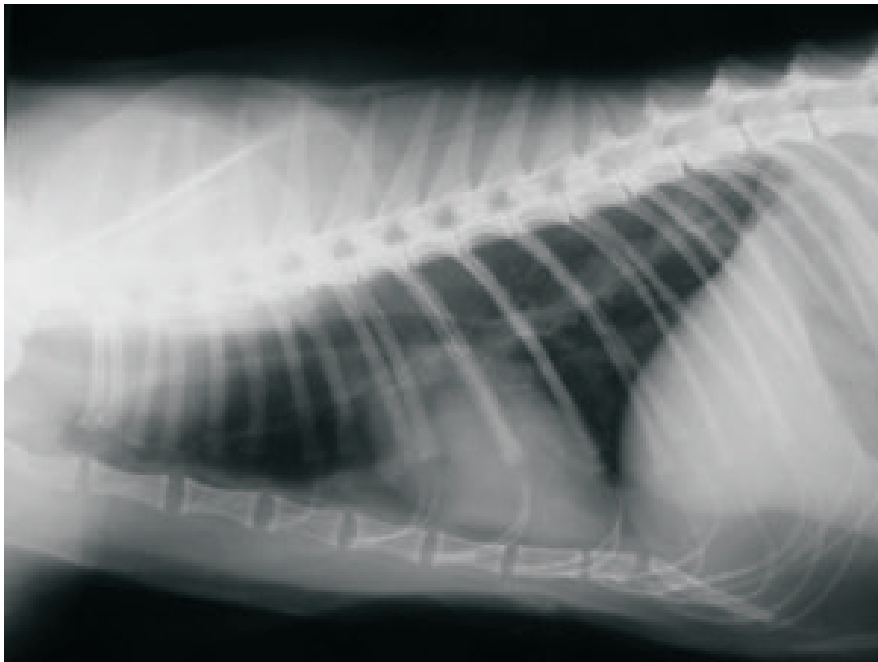


Figure 10: thoracic radiograph (left lateral view) of a cat with acute dyspnea caused by HWD. A focal interstitial pattern (caudal lung lobes) was present. Courtesy of Luigi Venco.

Filariae sometimes can be seen in the right heart chambers, pulmonary artery or distal caudal vena cava by echocardiography (Diakou et al., 2019). The body wall of adult HW appears as double hyperechoic parallel lines (“railway lines”) because of reflection of ultrasound waves by the cuticle of the worm (Figure 11). However, diagnostic sensitivity is operator-dependent, quantification of the worm burden is difficult and false negative as well as false positive evaluations are possible (Venco et al., 2015).

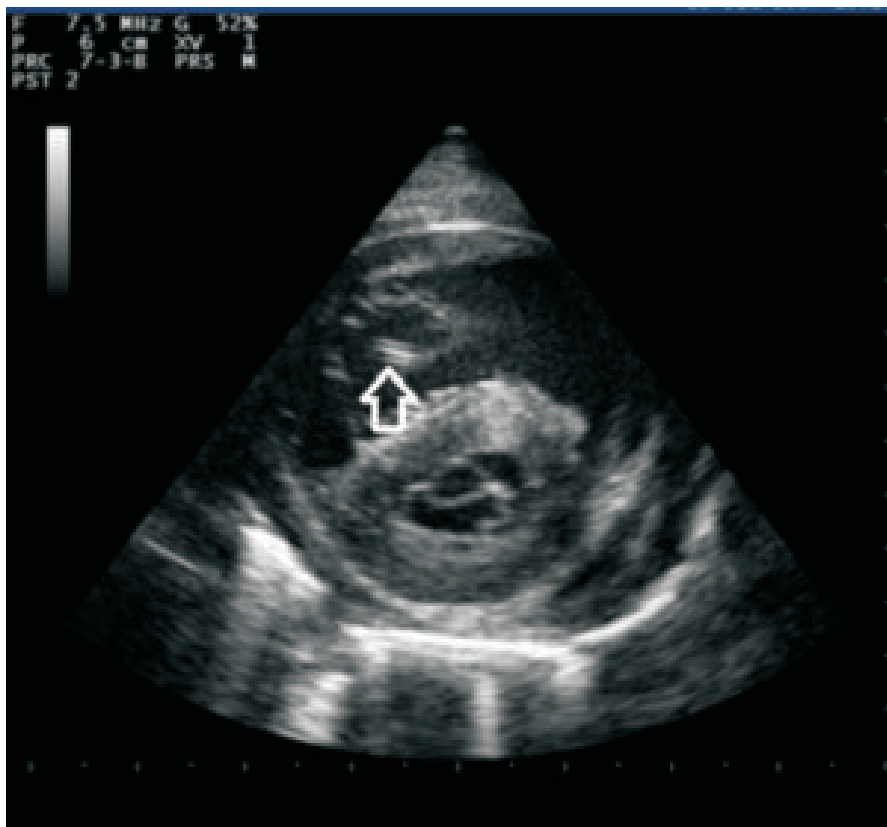


Figure 11: echocardiography, right parasternal short axis view, in a cat with HWD. The body wall of an adult HW appears as double hyperechoic parallel lines (arrow). Courtesy of Luigi Venco.

Necropsy is the only diagnostic method available in cases of sudden death but also to confirm the disease when negative results of ante mortem diagnostic methods are obtained in suspected cases (Biasato et al., 2017). In these cases, the right side of the heart, pulmonary arteries, and ectopic sites, including the brain and spinal cord in case of neurological signs, must be carefully examined for adult worms (McCall et al., 2008; Simón et al., 2012; Jones et al., 2014).

With respect to subcutaneous dirofilariosis, in a recent case CT features of nodules caused by *D. repens* were compatible with the diagnosis of metastatic fibrosarcoma and the unexpected diagnosis of subcutaneous dirofilariosis was obtained by the cytological assessment revealing the presence of both adult worms and microfilariae (Figures 12-14) (Manzocchi et al., 2017). Ultrasonographic examination of the nodules evidenced hyperechoic lines compatible with filarial nematode parasites (Figure 15) (Manzocchi et al., 2017).



Figure 12: computed Tomography (CT) image of the nodule in figure 7. An ovular neoformation is visible in the subcutis of the trunk (red arrow). Courtesy of Simone Manzocchi.

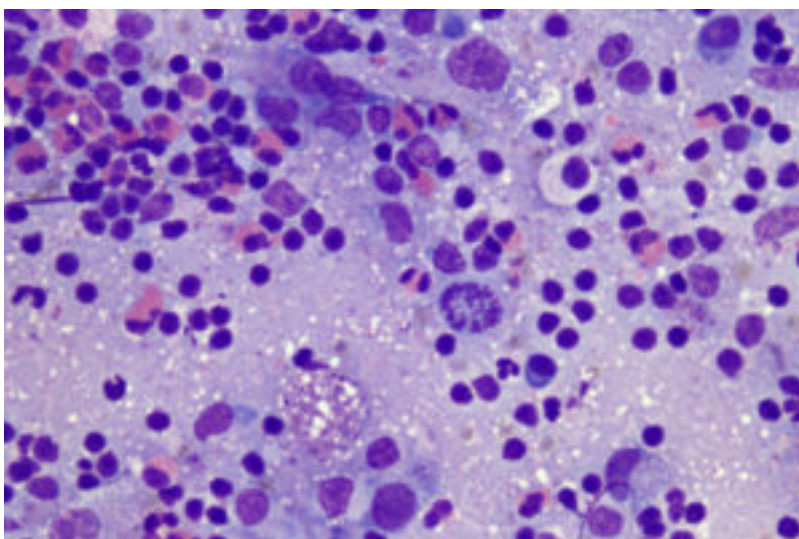


Figure 13: fine needle aspiration of the nodule in figure 7. Mixed inflammatory

population with prevalence of the small lymphocytes, eosinophils, and macrophages. May Grünwald-Giemsa. 40 X objective. Courtesy of Simone Manzocchi.

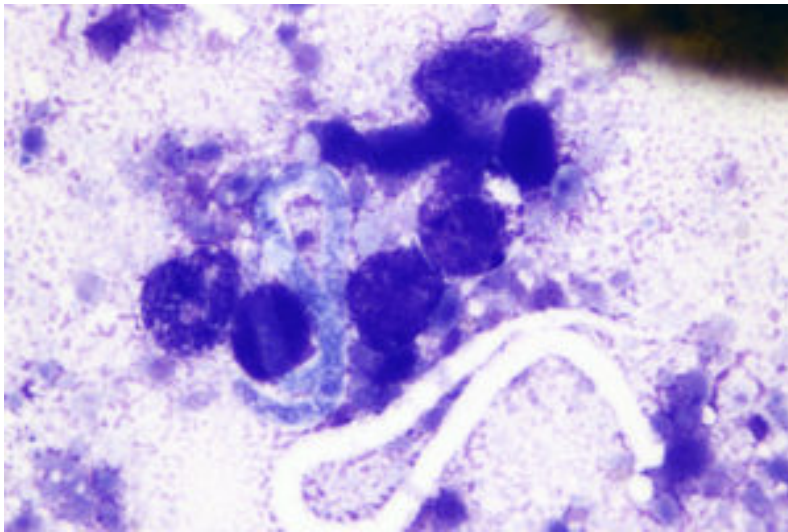


Figure 14: fine needle aspiration of the nodule in figure 7. One microfilaria admixed with several round morulated eggs is present. May Grünwald-Giemsa. 60 X objective. Courtesy of Simone Manzocchi.

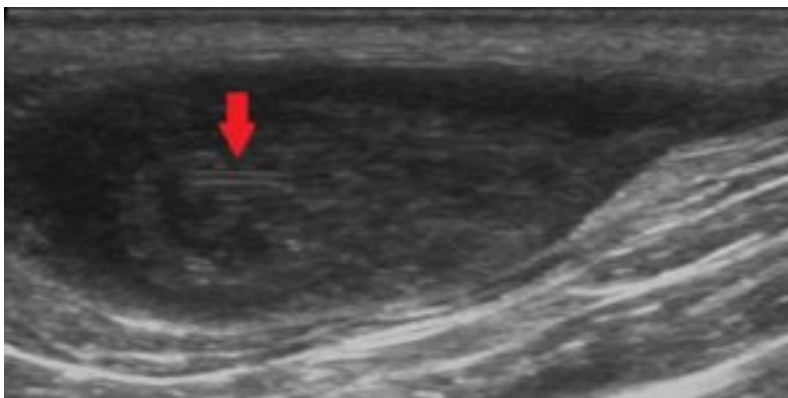


Figure 15: ultrasound image of the nodule in figure 7. Many double and parallel hyperechoic lines are visible. Courtesy of Simone Manzocchi.

Molecular investigations can be performed on DNA obtained from blood and collected worms. Parasite-species-specific PCR assays are available for discriminating *D. immitis* and *D. repens* (Favia et al., 1996). A panfilarial-6-species PCR has been developed and, in some cats, DNA of filarial worms not yet reported in feline hosts was detected (Rishniw et al., 2006; Manzocchi et al., 2017).

Treatment and follow-up

There is no adulticidal drug approved for the treatment of feline HWD, and adulticide therapy is not recommended in asymptomatic cats because self-cure occurs in most cases in 18-48 months (Venco et al., 2008; Jones et al., 2014). Infected cats should be followed up by thoracic radiography, echocardiography, and antigen and antibody testing for decision making regarding treatment and to detect self-cure.

Prednisolone (2 mg/kg/24 hour declining over a few weeks) should be given to cats with respiratory signs that test positive on antigen and/or antibody testing (Jones et al., 2014). In asymptomatic cats with suggestive radiographic changes, prednisolone treatment should also be applied, and treatment should be followed up by the same clinical, radiographic and antigen/antibody testing method (Jones et al., 2014). Improvement of radiographic changes associated with previous positive antigen tests becoming negative are markers of recovery despite the persistence of positive antibody tests (Jones et al., 2014). Hyperacute cases of HWD require intensive care unit stabilization because of the risk of respiratory failure and shock.

Adulticide therapy used in dogs (melarsomine) is not safe in cats and carries a high risk of pulmonary thromboembolism and

anaphylactic reactions following parasite death in treated cats (Jones et al., 2014; Alho et al., 2016). Surgical procedures to mechanically remove the adult parasites have been proposed in symptomatic cats for retrieving worms visualized from the right heart and main pulmonary arteries, but they have to be removed intact to avoid anaphylaxis (Iizuka et al., 2009; Jones et al., 2014). Surgical removal of an adult heartworm migrated to the femoral artery was successfully obtained by direct access to the worm from the arteriotomy site (Oldach et al., 2018).

Slow kill protocols combining monthly administration of heartworm-preventative drugs combined with a one-month course of doxycycline therapy are used in dogs when melarsomine is contraindicated and is reported in cats (Diakou et al., 2019), but their efficacy and safety are unknown and therefore these protocols are not recommended (Savadelis et al., 2017). Nevertheless, all cats diagnosed with HWD should also undergo monthly application of preventative drugs (see below).

In a cat affected by subcutaneous dirofilariosis, nodules containing adult worms and microfilariae have been successfully removed surgically (Manzocchi et al., 2017). There is no adulticidal drug approved for the treatment of feline subcutaneous dirofilariosis.

Prevention

Because of the unpredictable and potentially fatal course of HWD in cats and the lack of safe and effective treatments in endemic areas, all cats – irrespective of their access to outdoors – should be given monthly chemoprophylaxis from 2 months of age all year long for killing infective larvae in the L3-L4 stages (Jones et al., 2014). Although a recent study found that outdoor cats had a 3-fold increased risk of being *D. immitis* antigen-positive, it is known that about one third of all antigen-positive cats actually live indoors (Levy et al., 2017). The same recommendation is given for cats that live in areas that do not have heartworm but that are travelling to endemic areas. Chemoprophylaxis should be performed within 30 days of arrival in the risk area (European Scientific Counsel Companion Animal Parasites, 2012; European Society of Dirofilariosis and Angiostrongylosis, 2017). Unfortunately, awareness of the importance of feline HWD prevention seems to be low and is often neglected, especially in cat shelters, for economic reasons (Polak and Smith-Blackmore, 2014; Levy et al., 2017; Genchi et al., 2019).

Adequate preventative treatment covering the whole of the transmission season is crucial for effective prevention, and a year-round approach is often the best option because of climatic differences concerning humidity having a great impact on the risk of exposure for susceptible hosts (Montoya-Alonso et al., 2016). Five preventative drugs are currently available for cats and are monthly given orally or topically as spot-ons (Baker et al., 2014; Dillon et al., 2014; Little et al., 2015; McTier et al., 2019) (table 1). Antigen- or antibody-positive cats can be safely given preventative therapy, but both tests should be carried out before starting chemoprophylaxis to obtain a risk assessment for HWD in cats living in endemic areas (Jones et al., 2014).

Selamectin administration was not effective in preventing subcutaneous dirofilariosis in one cat but this apparent failure could have been due to it being stopped before the end of transmission season (Manzocchi et al., 2017).

Table 1: drugs available for chemoprophylaxis of feline HWD

MACROCYCLIC LACTONE	MONTHLY POSOLOGY	ADMINISTRATION ROUTE
IVERMECTIN	24 µg/kg	orally
MILBEMYCIN OXIME (in combination with praziquantel)	2.0 mg/kg	orally
MOXIDECTIN (in combination with imidacloprid)	1.0 mg/kg	topically spot-on
SELAMECTIN (may be in combination with sarolaner)	6.0 mg/kg	topically spot-on
EPRINOMECTIN (in combination with praziquantel & S-methoprene & fipronil)	0.48 mg/kg	topically spot-on

One Health

There is great interest in dirofilariosis because of the increasing number of human case reports in endemic areas. Immature *D.*

immitis worms can reside in a branch of pulmonary artery of humans and induce the development of pulmonary nodules (Simón et al., 2012). *Dirofilaria repens* can cause dermatitis or subcutaneous, submucosal, mammary, genital, omental, ocular or lung nodules, which can be misdiagnosed as malignancy (Pampiglione et al., 2001). The disease is sporadic and in Europe *D. repens* is responsible for human dirofilariasis more frequently than *D. immitis*, even in areas of high endemicity of the latter species (Simón et al., 2012; Capelli et al., 2018). Italy, France, Czech Republic, Serbia, Greece, and Ukraine are the countries where human dirofilariasis caused by *D. repens* is more frequent (Capelli et al., 2018). Epidemiological studies detecting antibodies in people found that rates of infection are similar as those of dogs in an endemic area (Simón et al., 2012).

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