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CLINICAL REVIEW

FELINE ASTHMA AND HEARTWORM DISEASE
Clinical features, diagnostics and therapeutics

Sarah Garrity, Tekla Lee-Fowler and Carol Reinero

Practical relevance: For feline practitioners, the cat with a cough or respiratory distress and thoracic radiographs with a bronchial or bronchointerstitial pattern suggests lower airway disease. Two important differentials, allergic asthma and heartworm disease (HWD), have many overlapping clinicopathologic features, but also clear and important differences in terms of cause and disease progression, treatment and prognosis. Notably, asthma is readily treatable and HWD is preventable.

Clinical significance: Feline HWD comprises two clinical syndromes: the comparatively recently described heartworm-associated respiratory disease (HARD) and adult HWD. The former is much more common; very few cats with HARD develop adult HWD. In HARD, following death of immature worms, pulmonary lesions may improve over time ('self-cure'). Lesions of adult HWD also improve over time as long as reinfection does not occur; however, with death of adult heartworms, mortality is high, and the prognosis is guarded. In asthma, morbidity is relatively high, but mortality is low, with an overall good to excellent prognosis.

Disease recognition: Feline asthma is encountered worldwide. In the authors' impression, feline HWD is often under-recognized.

Aims: The aim of this review is to assist clinicians in differentiating feline asthma from feline HWD; as such, the emphasis is on distinguishing clinical features, as well as on diagnostics, therapy and prognosis. In differentiating these conditions, clinicians can attempt the goal of properly managing these diseases and can best educate owners on prognosis.

Evidence base: For both feline asthma and feline HWD, the authors have drawn on the available peer-reviewed literature studies involving experimental models as well as spontaneous disease.

Keywords: *Dirofilaria immitus*; lower airway disease; allergy; thoracic imaging

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Definitions and pathogenesis

Asthma

Feline asthma is a chronic respiratory disorder characterized by eosinophilic airway inflammation, airway hyperresponsiveness, airflow limitation and airway remodeling.[1] Similar to what is noted in humans, aeroallergens activate Th2 lymphocytes, which produce cytokines capable of orchestrating the allergic inflammatory response.[1] Importantly, allergen-specific immunoglobulin E (IgE) binds avidly to receptors on mast cells and basophils. Upon subsequent re-exposure to the aeroallergen, degranulation of mast cells and basophils further promotes the inflammatory response, resulting in the aforementioned pathological signs of asthma.[2] Progressive structural changes result from recurrent, chronic exposure to the allergen and may lead to a decline in lung function over time. Due to bronchoconstriction, mucus plugging of airways and airway wall remodeling/edema, asthma is considered an obstructive lung disease.

Asthma is caused by inhalation of allergens, driving a hypersensitivity response to what should be benign substances.

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Heartworm disease

Feline heartworm disease (HWD) results from infection with the filarial nematode *Dirofilaria immitis*. Although the dog is the final host and natural reservoir, cats can also be infected and develop disease related to immature worms (heartworm-associated respiratory disease [HARD]; common) or adult worms (adult HWD; rare). The prevalence of feline HWD is suspected to be 5–10% of that of canine HWD in any area,[3] but has been reported to be as high as 20%.[4]

Mosquitoes carry the third-stage larvae and transmit them through the host's skin, whereafter there is further development in the subcutaneous tissues. After molting to fourth-stage larvae and then young adult stages, the worms migrate to the pulmonary arteries/arterioles 70–90 days post-infection. Death of immature worms incites an intense inflammatory response leading to airway, interstitial and vascular changes in the pulmonary parenchyma.[5,6] Importantly, assuming no reinfection, these lesions of HARD show progressive improvement, starting 6–8 months post-infection; over time there appears to be substantial reversibility of lesions.[6] One study determined that by 18 months post-infection, there was no significant difference in the histologic grading of airways, interstitium or arteries/arterioles between cats treated with selamectin 28 days post-infection (in which 'pre-cardiac' third- and fourth-stage larvae were present but immature adults were killed before reaching the pulmonary arteries, thus no HARD) and cats with HARD.[6] However, there was tremendous variation between cats and within lung lobes of individual cats, with some cats having lesions present, just more interspersed rather than uniform.[6] The clinical implications of these chronic lesions is unknown but suspected to be minimal.

Although the vast majority of immature worms are killed by the cat's immune system, in a small percentage of cases immature worms become adults, leading to adult HWD. In general, worm burden is low (usually 1–2 worms, sometimes of the same sex), and patent infections leading to microfilaremia are rare and transient.[7] In both HARD and disease due to adult heartworms, similar histopathologic changes occur in the airways, interstitium and vasculature in the early stages (up to 8 months).[5] Adult heartworms, in marked contrast to immature worms, suppress the feline immune system, leading to a relative anti-inflammatory state that minimizes the development of clinical signs.[8,9] This can occur despite striking radiographic/CT and histologic lesions.[5,6,10] While these lesions are more pronounced than in cats with HARD alone, lesions also improve over time as long as reinfection does not occur.[6] Adult heartworms typically live for only 2–4 years in cats.[4,11–13] When they die, intense inflammation and thromboembolism can occur, sometimes leading to acute death of the cat.[7]

It has been suggested that HARD and adult HWD are restrictive lung disorders (due to fibrosis), with studies documenting that despite airway wall thickening, there is no airway hyperresponsiveness in response to agonists and airways are refractory to relaxation (ie, they are 'stiff').[10,14] Results of CT scans in cats with disease due to the presence of adult *D immitis* support the finding of restrictive lung disease, with patchy increases in lung opacity and lower lung volumes with absence of hyperinflation.[10]

Experimental modeling – feline asthma and heartworm disease

Much of what is known about the pathogenesis of feline asthma is derived experimentally from feline models of allergic asthma.[15,16] Similarly, much of the understanding of the pathology of HARD and adult HWD comes from experimental feline models. The typical model for HARD is based on a single, high dose infection of 100 *D immitis* third-stage larvae.[5,6,10] In nature, cats would be unlikely to have a single infection of this magnitude and are much more likely to have repeated cumulative infections. While the model still has relevance in terms of the lesions produced and pathologic changes over time, it should be noted that it may not represent natural infection and the typical disease course.

The vast majority of immature worms are killed by the cat's immune system, but in a small percentage of cases immature worms become adults, leading to adult heartworm disease.

Discriminating between asthma and heartworm disease

Discriminating between asthma and HWD can be challenging. Diagnosis depends on a comprehensive evaluation incorporating signalment, history, clinical signs, diagnostic imaging, blood tests for heartworm infection and various other ancillary tests.

Signalment, history and clinical signs

Feline asthma is a disease first noted in young to middle-aged cats without a gender predilection, with the Siamese breed suggested to be over-represented in some studies.[1,17,18] While the median age is 4–5 years at presentation for veterinary care,[18,19] most cats have had chronic signs suggesting an even earlier time of onset. Careful questioning regarding use of chemoprophylaxis for the prevention of heartworm infection is critical; if cats have had appropriate administration of medication, this is strong evidence to rule out heartworm-associated disease as the cause of the asthma-like signs observed.

In stable asthmatic cats, the classic history is chronic and/or episodic with complaints of cough, wheeze and increased respiratory rate or effort. Depending on exposure to sensitizing allergen(s), clinical signs frequently wax and wane, with periods of normalcy in between. Thus a normal physical examination does not rule out asthma. Cats may also present for suspected gastrointestinal signs; typically an owner perceives their cat is trying to vomit hairballs, but it is in fact coughing. Most of these cats have paroxysmal bouts of coughing immediately preceding vomiting; they may also fail to bring up vomitus despite their efforts, which owners perceive as dry-heaving.

Asthmatic cats with an unstable presentation ('status asthmaticus') present in crisis with open-mouth breathing, tachypnea and/or increased expiratory effort with an abdominal 'push'.[1] On physical examination, a spontaneous or inducible cough may be noted, with wheezing, tachypnea or expiratory respiratory distress.

Clinical signs of feline HWD depend on the stage of infection and response of the host. Cats of any age can be bitten by infective mosquitoes with a lag period prior to clinical signs of HARD. As asthmatic cats generally have an initial onset of clinical signs at an early age, the index of suspicion for heartworm infection would be higher when clinical signs are first noted in an older cat. Despite owners' perception to the contrary, heartworm infection can occur in cats housed in indoor environments, with studies documenting between 19% and 27% of all confirmed cases being cats living indoors only (reviewed in Litster et al);[3] thus an indoor environment cannot be used to rule out heartworm infection.

Clinical signs in HARD vary in severity and type, ranging from asymptomatic to signs of lethargy, coughing, tachypnea and respiratory distress.[3] Respiratory distress is generally mixed, with increased effort both on inspiratory and expiratory phases, and not predominantly expiratory distress as in feline asthma. An acute onset of inspiratory distress might indicate laryngeal edema from anaphylaxis with acute worm death. Vomiting and weight loss have also been reported in cats infected with adult *D immitis*.[7,8,20] Neurologic signs can be seen with aberrant parasite migration.[20]

Why differentiate between asthma and heartworm disease?

It has been suggested that there is no good reason to discriminate between feline asthma and the two major syndromes that heartworm infections cause in cats due to the testing being non-specific, treatment being identical and prognosis not being impacted by the diagnosis.[21] Admittedly, it can be difficult to determine the outcome for cats with either asthma or feline heartworm infection, but as asthma is readily treatable and HARD/adult HWD is preventable, discrimination should be attempted. Indeed, when examined in depth, it is obvious that both feline asthma and the diseases associated with infections with larval or adult heartworms are distinct entities. With care, asthma and heartworm infection can be differentiated with the goal of properly managing these diseases, which have distinctly different causes and can have markedly different outcomes that should be explained to the owner.

Heartworm infection can occur in cats living indoors only. Thus an indoor environment cannot be used to rule out heartworm disease.

In cats with adult heartworms, clinical signs of HARD may dissipate over time, and suppression of the immune system induced by adult worms may lead to an asymptomatic phase.[8,9] However, a subpopulation of cats may continue to have chronic histologic lesions, as noted earlier. Peracute signs can include respiratory distress, hemoptysis, syncope, ataxia and/or seizures, underscoring involvement of the respiratory, gastrointestinal and neurologic systems.[4,8] Acute death syndrome is also common in cats harboring adult heartworms.[4,3,7,11]

Diagnostic imaging

Thoracic radiography

In cats with a history or physical examination supportive of respiratory disease, thoracic radiography is one of the most important initial diagnostic tests to discriminate cardiac from respiratory disease and identify the presence, anatomic location and severity of lesions. Despite some overlapping radiographic features, there are some characteristics that are more strongly supportive of either asthma or disease associated with heartworm infection.

Typical thoracic radiographic findings in stable feline asthmatics range from unremarkable radiographs to a diffuse bronchial or bronchointerstitial pattern.[17–19] Lobar collapse, most frequently involving the right middle and the caudal portion of the left cranial lung lobes, is noted in some asthmatic cats (Figure 1).[1,17,19] This likely occurs secondarily to mucus hypersecretion obstructing the lobar bronchi and leading to downstream atelectasis.[1] Rarely, bronchiectasis, nodular lesions or pneumothorax have been reported, although these should not be considered typical of asthma. In one study, bronchiectasis and nodular lesions were described in cats with various types of feline bronchial disease including chronic bronchitis and parasitic bronchitis.[22] Separately, in a retrospective study of cats with spontaneous pneumothorax, 4/16 cats had concurrent asthma; it is unclear if asthma was the cause of the pneumothorax or a comorbid condition.[23] In cats with status asthmaticus, hyperinflation is a prominent finding superimposed on the aforementioned findings. Resolution of hyperinflation (at least in part) on subsequent radiographs, after treatment with a bronchodilator, would be strongly supportive of a diagnosis of asthma.[2]

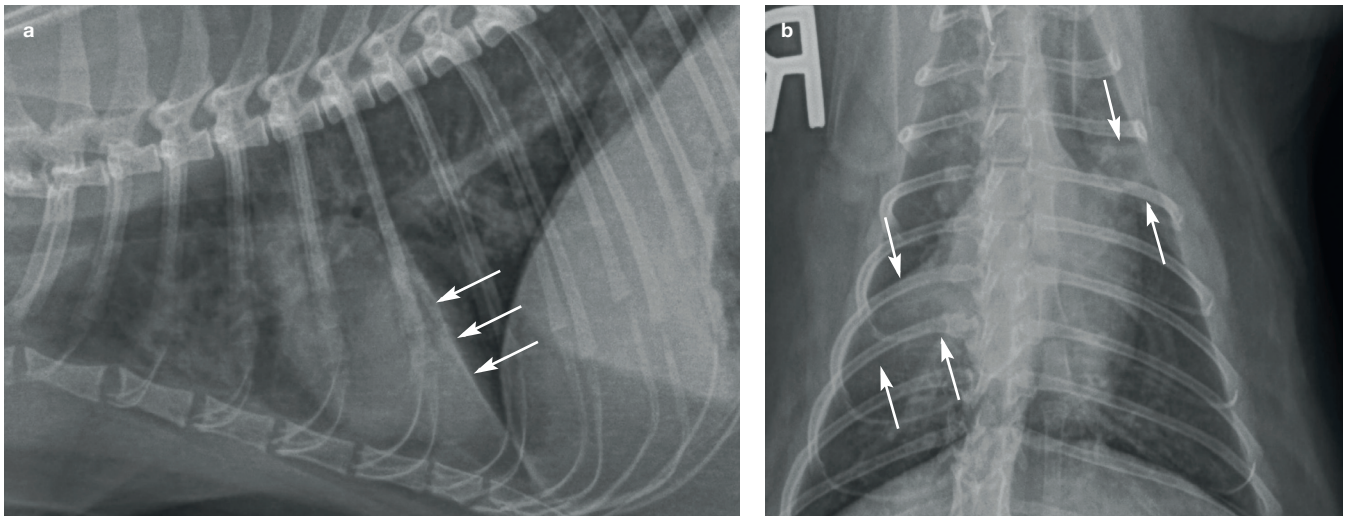

Figure 1 (a,b) Orthogonal views of the thorax from a cat with asthma. A diffuse bronchointerstitial pattern is noted in addition to atelectasis of the right middle and caudal portion of the left cranial lung lobes. Lobar borders are delimited by arrows

Description of thoracic radiographic features in feline heartworm infection poses challenges (see box). Notwithstanding, common radiographic changes in pet cats with HWD have been described and include lobar and peripheral pulmonary artery enlargement and a bronchointerstitial pattern that can be patchy or diffuse and is most prominent in the caudal lung lobes.[11,24,25] A ratio of the width of the right pulmonary artery to the width of the 9th rib (using a dorsoventral or ventrodorsal view) greater than 1.6 would be strongly suggestive of heartworm infection.[26] While much less common, enlargement of the cardiac silhouette, lobar consolidation, focal opacities, pleural effusion, pulmonary hyperinflation, pneumothorax and evidence of thromboembolism have been described;[4,11] however, these should not be considered typical changes of feline heartworm infection. As with asthma, thoracic radiographs in feline heartworm infection can be non-specific and may not show any overt abnormalities.[11,24]

As with asthma, thoracic radiographs in feline heartworm infection can be non-specific and may not show any overt abnormalities.

Experimental models of HARD and of adult heartworm infection allow for comparison of radiographic lesions between these two syndromes.[5] While important to keep in mind that the presence of the response in the lungs to the existing adult heartworms was preceded by HARD, radiographs from cats with HARD alone vs adult HWD were indistinguishable from each other at the later time points of one study.[5] Experimental infection using venotomy for transplantation of *D immitis* to study the effects of a heartworm infection without prior HARD did cause bronchointerstitial patterns[5] and, when arteriography was performed, demonstrated tortuous caudal arteries with aneurysms and regions of lung lacking perfusion.[27] In both studies changes were most prominent in the caudal lung lobes.

Thoracic radiographic features of feline HWD: current limitations on understanding

As described below, there are a number of challenges that have hampered understanding of what are typical radiographic lesions of feline heartworm infection.

- There is no reliable criterion standard for diagnosis of HARD, and in some cases where cats have adult heartworms the infection may be missed when antigen tests, echocardiography and/or necropsy fail to identify adult worms. Thus, it is difficult to perform clinical studies when the patient population cannot be clearly defined.
- Radiographic lesions of HARD and disease due to adult heartworms are generally grouped together, as much of the emphasis in the literature has been on feline infections with adult heartworms, and HARD is a comparatively recently described syndrome.[4,5] While adult heartworm disease is a sequela of HARD (cats may either have concurrent HARD or be in a recovery phase of HARD), few cats with HARD will go on to develop adult heartworms.
- Radiographic lesions of feline heartworm infection are dynamic with time.[24]
- Importantly, nearly all of the studies performed in pet cats with heartworm infection have failed to rigorously eliminate other respiratory disorders including feline bronchial disease (ie, asthma, chronic bronchitis and other types of parasitic bronchitis), infectious pneumonia and cardiac disease. Thus, radiographic lesions could have been caused by other types of pathology instead of, or concurrent with, HARD or adult heartworm infection.

Echocardiography

Echocardiography is useful to help clarify if cardiovascular changes are due to the presence of adult heartworms or another primary cardiovascular disorder. It may be the only way to definitively diagnose the presence of worms ante mortem.[28] However, operator experience and skill can play a significant role in worm identification: sensitivity of echocardiography ranges from 40–100% depending on the examiner.[28] Worms, which appear as parallel hyperechoic lines, are most often found in the pulmonary arteries, and occasionally in the right atrium, right ventricle and vena cava.[7,28] Absence of worms on echocardiography does not rule out HWD. False positive results due to artefacts or imaging of the right ventricular chordae tendineae are also possible.[7,29] While pulmonary hypertension has been reported with heartworm infection, it is rare.[27]

Computed tomography

CT has been used much less frequently than the above imaging tests to characterize changes noted in asthma and heartworm infections, despite the improved sensitivity of this modality for detecting lesions as compared with radiography.

In cats with naturally developing asthma, subjective and objective measures of bronchial wall thickness were increased compared with healthy controls in two studies;[30,31] in asthmatic pet cats, lesions were diffuse and, overall, there were increases in lung attenuation.[30] Experimentally asthmatic cats had CT scans showing increased bronchial wall thickening, ground-glass opacity, consolidation and parenchymal bands.[32] All pet and experimentally asthmatic cats were stable at the time of imaging (ie, not in crisis), likely explaining the lack of air trapping.

Two case reports have described CT angiography in pet cats with adult heartworms: lesions included diffuse ground-glass opacity in one cat, multifocal regions of consolidation or lobar consolidation (suspicious for infarcts) and filling defects in the pulmonary arteries (compatible with pulmonary embolism).[33,34] In cats experimentally infected with 100 third-stage larvae that were allowed to mature to adulthood, CT showed increases in peribronchovascular densities, a decrease in total lung volume and a lack of air trapping, supportive of restrictive lung disease.[10] Importantly, lesions were patchy, with severe changes adjacent to completely normal lung.

Blood tests for heartworm infection

A diagnosis of HARD and/or adult HWD requires multiple avenues of testing including antibody and antigen serology. Proper interpretation with an understanding of test limitations is necessary for an informed diagnosis.[4,7]

A positive antibody test indicates that a mosquito has successfully transmitted larvae but does not document the precise stage of heartworm development within the cat, and the duration of the antibody response can vary widely between cats.[4,8] Based on one study, when 100 third-stage larvae were injected into a group of cats, with or without use of preventives, 93% of cats had a positive antibody test at some collection point within a 245-day time period.[5] In a cat with appropriate clinicopathologic features of HARD and in which other disease mimics have been ruled out, a positive result would be strongly supportive of HARD.[10] As mentioned previously, there is a high mortality of immature worms. Therefore, few cats with HARD will go on to develop adult heartworms, and other diagnostic tests would be required for the definitive diagnosis of adult heartworm infection. With a negative antibody titer, neither HARD nor an adult heartworm infection can be definitively ruled out, although (in conjunction with other test results) the index of suspicion would be lower.[5,7]

A positive antigen test, indicative of the presence of adult female worm(s), is highly specific for diagnosis of adult heartworms and, by default, ongoing or resolving HARD.[7] False negative results may occur with immature worm burdens and male worm-only infections.[35] As HARD is far more common than adult heartworm infection in cats, a large number of heartworm antigen tests in cats bitten by infective mosquitoes and presenting with clinical signs compatible with either asthma or heartworm infection should be expected to be negative. Negative results do not rule out either HARD or adult heartworm infection, but, in conjunction with other tests, may put them lower on the differential list.[7] Heat treatment of serum samples may dissociate antigen–antibody complexes and allow for improved detection of heartworm antigen in cats.[36]

In feline adult HWD, fewer than 20% of cats have microfilaremia and it is only detectable for 1–2 months after a mature infection is present (7–8 months post-infection).[4,35] Thus, tests to detect microfilaremia, such as a modified Knott test, are considered unreliable and are not recommended. However, if microfilaremia is detected, as with a positive antigen test, it is considered a definitive test for adult heartworm infection (and, by default, HARD).[7]

Serology summary

- A positive antibody test can provide supportive evidence for HARD (or response to adult heartworms).
- A positive antigen test is a definitive test for the presence of adult heartworms in the cat.
- Negative antibody and antigen tests may decrease the index of suspicion for heartworm infection but do not rule out either HARD or adult HWD completely.

Ancillary diagnostics

Airway lavage cytology

The imaging tests discussed above are helpful for revealing patterns of disease to generate differential diagnoses; however, they do not provide a cytologic diagnosis. Bronchoalveolar lavage sampling is frequently performed in cats to more accurately classify the underlying lung pathology. Both asthma and heartworm infection will be associated with increased percentages of eosinophils (Figure 2); thus, aside from confirming airway eosinophilia,[10,37] the main value of bronchoalveolar lavage is to rule out disease mimics (eg, presence of *Aelurostrongylus* larvae, or non-septic suppurative inflammation in chronic bronchitis) and secondary bacterial infection.

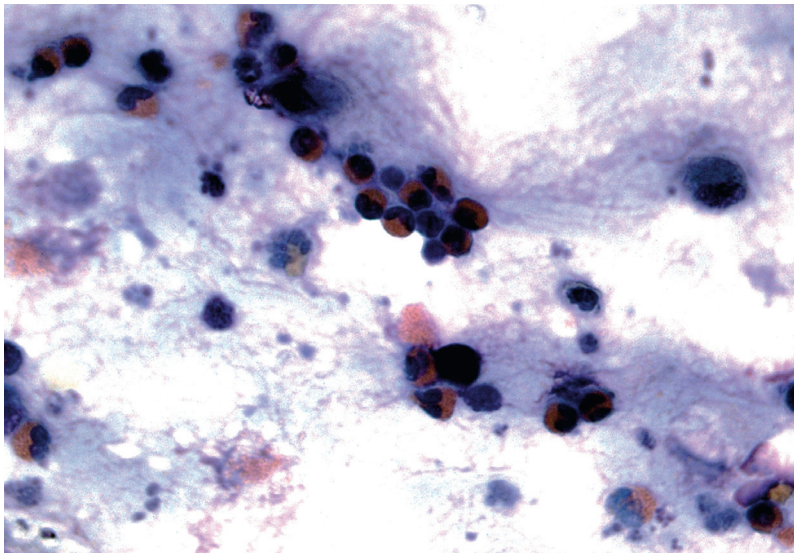

Figure 2 Bronchoalveolar lavage fluid cytology demonstrating airway eosinophilia and mucus hypersecretion

Allergen-specific IgE

In pet cats suspected to have asthma, positive results for allergen-specific IgE can increase the confidence of an allergic asthma diagnosis. Either intradermal testing or serum allergen-specific IgE measurement can be performed and both are considered highly specific.[38] Importantly, commercial serum testing methods are very different, with the enzymo-immunometric assay being completely unreliable.[38] An added benefit of identifying sensitizing allergens is the possibility of modulating the environment for allergen avoidance or diminished allergen contact as part of a long-term treatment plan.

Pulmonary function testing

In human medicine, pulmonary function testing is helpful to discriminate between obstructive and restrictive pulmonary disorders. As discussed, asthma is an obstructive airway disorder, and there is supportive evidence to indicate that heartworm infection is a restrictive disorder.[10]

Direct measurement of airway resistance is used rarely in cats as it currently requires general anesthesia and either dedicated research equipment or ventilators capable of pulmonary mechanics measurement.[15,39] In conscious cats, barometric whole body plethysmography (BWBP) has been used as a non-invasive surrogate marker for airflow limitation;[40] however, it is important to understand that this technique has been criticized as not being an indicator of true airway resistance.[41] Bronchoprovocation using aerosolized agonists to stimulate airway hyperresponsiveness, a hallmark feature of asthma, can provide additional supportive evidence, as has been shown in experimental and pet cats with asthma.[39,42] There is also in vitro evidence that feline asthmatic airways are hyperresponsive to agonists.[43]

Direct measurement of airway resistance in cats with HARD or adult heartworm infections has not been performed to the authors' knowledge. Likewise, bronchoprovocation has not been performed in tandem with BWBP in cats with presumptive HARD. One research group concluded resting measures of pulmonary mechanics (BWBP) without bronchoprovocation in cats with HARD were enough to support bronchoconstriction;[44] however, this may be an overinterpretation given the limitations of this non-invasive technique[41] and the finding needs to be substantiated by direct measures of airway resistance. Additionally, a majority of cats in the BWBP study had radiographic evidence of hyperinflation,[44] which, despite positive antibody titers to *D immitis*, begs the question of whether these cats were also asthmatic. These studies using BWBP are contradictory to findings in experimental heartworm infection where CT scans, as well as in vitro evaluation of relaxant and stimulant responses of bronchial smooth muscle,[10,14] strongly supported a restrictive lung disease with absence of airway smooth muscle responsiveness to agonists or antagonists.

In pet cats suspected to have asthma, positive results for allergen-specific IgE can increase the confidence of allergic asthma diagnosis.

Treatment

Asthma

Treatment for asthma aims to control clinical signs and decrease future exacerbations. The cornerstone of treatment for stable asthmatic cats is environmental modulation, weight management, glucocorticoids and, in some cases, bronchodilators.[1] Environmental modulation includes minimizing exposure to nonspecific irritants (smoke, aerosols, dust, etc), allergen avoidance when possible and use of high-efficiency particulate air filters for indoor cats.[45] Glucocorticoids (oral or inhaled [Figure 3][3,42,45,46]) are critical to attenuate inflammatory airway disease, thus diminishing airway hyperresponsiveness and progressive remodeling. They need to be administered lifelong, even in asymptomatic cats, although they can be tapered to the lowest effective dose controlling clinical signs.[47] Bronchodilators reverse smooth muscle contraction mediated by allergens or irritants, and are helpful in cats with clinically relevant airflow limitation.[2] They can be used when stable cats fail to respond to glucocorticoids alone, although as they lack substantial anti-inflammatory properties, they should never be given as monotherapy.[2] Not all stable asthmatic cats will need bronchodilators.

In unstable asthmatics, the single-most critical drug is a bronchodilator; supplemental oxygenation, glucocorticoid therapy and placing the cat in a secluded environment to reduce stress are also important treatment measures.[19] An injectable short-acting beta-2 agonist such as terbutaline is preferred by the authors in cats with status asthmaticus as bronchospasm limits delivery of inhaled bronchodilators to the lower airways.[48] Once the life-threatening crisis has passed, these cats are managed as stable asthmatics. For additional information on feline asthma treatment, including research on novel therapies, the reader is referred to other reviews.[1,2]

Figure 3 To minimize systemic effects, inhalant glucocorticoids administered using a spacer with a tight fitting face mask are an excellent alternative to oral glucocorticoids

While in unstable asthmatics the single-most critical drug is a bronchodilator, not all stable asthmatic cats will need bronchodilators.

Heartworm disease

Feline HWD is a completely preventable disease if appropriate chemoprophylaxis is used.[10] Regardless, if HARD or adult infection is diagnosed, chemoprophylaxis should be started to prevent subsequent infection as the cat is attempting a 'self-cure'.[4] Given evidence of the efficacy of moxidectin and selamectin in targeting immature worms responsible for HARD,[5,49] these are preferred by the authors over ivermectin and milbemycin, although all are effective in preventing adult heartworm infections. Routine chemoprophylaxis is advocated for any cat in an endemic area.

For cats with HARD that are displaying clinical signs or more marked changes on thoracic radiography, short tapering courses of glucocorticoids are recommended.[4,7] If clinical signs of HARD are severe, oxygen supplementation and injectable glucocorticoids would seem prudent.[7] While bronchodilators have been advocated, research in experimental feline HARD suggests that airways would not respond to this treatment (see earlier discussion on 'Pulmonary function testing').[5] For cats that are infected with adult heartworms and are clinically stable, treatment as for HARD is advocated. Cats presenting with peracute/acute signs of anaphylaxis should be stabilized with epinephrine, fluid therapy and glucocorticoids.[13,50]

Adulticides are discouraged in cats because the death of adult worms may result in anaphylaxis, thromboembolism and death of the feline host; additionally, melarsomine is potentially toxic in cats.[7] The use of doxycycline in cats to rid heartworms of the obligate endosymbiont bacteria *Wolbachia* is still being evaluated but at this time is not a recommended treatment. Surgical removal of heartworms can be performed; however, if the worm breaks, or pieces of the cuticle are lost, acute anaphylaxis and sudden death can occur.[51] Therefore, surgery is not routinely recommended.

Routine chemoprophylaxis is advocated for any cat in areas endemic for heartworm disease.

Prognosis

Asthma

Median survival times are not well described for pet cats with asthma, although asthma is generally thought of as a disease with much higher morbidity than mortality. A lack of appropriate therapy (eg, antibiotics alone[19]) and failure to use anti-inflammatory doses of glucocorticoids lifelong likely explains some treatment failures and subsequent euthanasia. Currently, all therapies are palliative and, while there is no cure, asthma is a disease that can be successfully managed for years.[2] As with adult HWD, sudden death can occur in asthma; thus, aggressive treatment of airway inflammation and airway hyperresponsiveness is critical. Although tapering the glucocorticoid to the lowest effective dose to control clinical signs is a standard recommendation, one study documented persistent airway inflammation in symptom-free cats receiving high doses of steroids,[47] underscoring the need for future studies to guide treatment recommendations. Persistence of airway inflammation contributes to progressive remodeling of the lung and declines in lung function over time.

Heartworm disease

The natural course of HARD in pet cats is challenging to study because of the difficulty in establishing a definitive diagnosis without a criterion standard test; thus, the prognosis is unclear. In comparison, the prognosis for any cat with adult heartworm infection is considered guarded and sudden death of the cat may occur. With death of adult heartworms, host mortality is high, with death rates ranging from 21–47%.[3,7,12] In cats exhibiting clinical signs, one study documented a median survival time of 1.5 years, with cats living past the first day of presentation having an increase in median survival time to 4 years.[20] Only 18% of cats in this study were considered survivors of their adult heartworms, having outlived the heartworms.[20] Two additional studies in asymptomatic cats showed 79–82% were considered to have self-cured, with 18–21% dying during long-term follow up.[12,13] With active infection with adult heartworms, there is no way to prevent sudden death of the cat. The only option is to prevent subsequent infection by using chemoprophylaxis if the cat outlives the heartworms.

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KEY POINTS

- Asthma is caused by inhalation of allergens, driving a hypersensitivity response to what should be benign substances. Heartworm disease is caused by a host pulmonary immune response to eliminate either immature *D immitus* worms (HARD) or adult heartworms.
- Asthma is a classic example of an obstructive lung disease, whereas cats with heartworm infection have a phenotype more closely resembling restrictive lung disease.
- Despite challenges in discriminating feline asthma from heartworm disease, there are clear differences between these two diseases relevant for prevention, treatment and prognosis.
- Cats presenting in expiratory respiratory distress are almost certainly asthmatics; acute inspiratory respiratory distress is more compatible with anaphylaxis from a dying adult heartworm.
- Cats presenting with clinical signs for the first time at an older age are less likely to be asthmatic.
- Radiographic features strongly supportive of asthma include lobar collapse and reversible hyperinflation in response to a bronchodilator. Features supportive of heartworm infection include vascular changes and focal or multifocal lung opacities.
- Echocardiography may identify adult heartworms, but is operator dependent.
- An understanding of what is learned from serologically testing cats for antibodies to heartworms or directly detecting heartworm antigen is an integral part of an informed diagnosis.
- Asthma is considered progressive and incurable, but highly treatable. The best approach to treatment is use of lifelong glucocorticoids with environmental modulation, weight management and, in some cases, bronchodilators.
- The optimal approach to prevent disease associated with heartworm infection is use of an appropriate chemoprophylactic.
- Because feline heartworm infection can mimic many features of asthma, and because it is possible for both diseases to occur in the same cat, administration of a chemoprophylactic is prudent in any cat suspected of either disease.
- Feline HARD and disease associated with adult heartworms may slowly improve over time after apparent 'self-cure'.
- Treatment of HWD focuses on controlling clinical signs.

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