HEARTWORM disease, caused by *Dirofilaria* species, occurs almost everywhere its vector, the mosquito, is found.

Locations include the United States (excluding Alaska), regions of Canada, South America, southern Europe, south-east Asia, the Middle East, Australia and Japan. This article will focus on the diagnosis, chemoprophylaxis and treatment of heartworm disease in dogs and cats.

**Diagnosis in dogs**

Commercial serological tests identifying antigens to the adult female heartworm are the most sensitive method for screening a population of asymptomatic dogs or verifying infection. Antigen tests identify most “occult” (microfilaria-negative) infections consisting of at least one mature female worm, and are almost 100 per cent specific. Tests identifying the presence of antibodies to the larval form appear to be of limited value in dogs.

Antigen tests show minor variations in sensitivity, but equally high specificity. Reliable results require strict compliance with the manufacturer’s instructions. False-positive results are usually due to technical error and most test manufacturers will analyse ambiguous samples in their own laboratories. If the history rules out significant potential for exposure, positive antigen tests in asymptomatic dogs should be confirmed by other means prior to initiating adulticide therapy.
False-negative test results occur when infections are light, female worms are immature, only male worms are present and/or the test kit or sample has not been warmed. Negative results should be interpreted in the light of clinical evidence and exposure history.

Microfilariae can be visualised microscopically in fresh blood, or beneath the buffy coat in a microhaematocrit tube when high numbers are present. Lower numbers (50/ml to 100/ml) may be missed unless a concentration technique is used (either a modified Knott’s test or filtration test). The modified Knott’s test is the preferred method for differentiating *D. immitis* from non-pathogenic filarial species.

Effective screening requires optimal timing. In most dogs, antigen is detectable from five months and microfilariae from 6.5 months post-infection. When worm burdens are low or animals are receiving macrocyclic lactones, antigenaemia may not be detectable until nine months post-infection. The interval between infection and the likely appearance of microfilariae is the pre-patent period and averages seven months. Dogs younger than seven months of age do not require testing; older dogs should be tested approximately seven months following the date of potential exposure.

Unprotected dogs more than seven months of age – or dogs in which there is a suspected breach in dosing compliance for three or more months – should be tested for antigen prior to starting or resuming preventive therapy, and again at four and nine months after initiating prophylaxis. A similar testing protocol is recommended when compliance has been good and the owner wishes to change the chemoprophylaxis.

Monthly chemoprophylaxis using one of the macrocyclic lactones will eliminate microfilariae by various mechanisms within six to 12 months of oral dosing, or one month following moxidectin slow-release injection. Antigen testing is the most reliable method of retesting these dogs. Lack of efficacy has been reported for all macrocyclic lactones, and annual retesting is recommended to ensure that prophylaxis is being achieved.

When daily diethylcarbamazine citrate (DEC) is used for chemoprophylaxis, there is a greater risk of breaks in treatment. Should a patent infection develop, these dogs are at risk of potentially fatal reactions following resumption of DEC. For this reason, a microfilaria test must be run before resuming seasonal prophylaxis with this drug and then annually.

Additional testing methods are useful for confirming the diagnosis and staging the severity of heartworm disease. Radiography may demonstrate enlarged, tortuous and often truncated peripheral intralobar and interlobar branches of the pulmonary arteries, particularly in the diaphragmatic lobes, often accompanied by variable degrees of pulmonary parenchymal disease. Echocardiography can demonstrate evidence of heartworm infection and aid cardiac function assessment. In heavy infections, heartworms may be visible in the main pulmonary artery, right and proximal left interlobar branches, within the right side of the heart, and occasionally in the
orifice of the tricuspid valve.

**Diagnosis in cats**

The diagnosis of heartworm disease in cats may require the use of several tests. Circulating microfilariae are seldom found in infected cats, but may appear within 195 days of exposure. They rarely persist beyond 228 days due to host immune-mediated mechanisms.

Antigen tests are less reliable, because infections consisting of only male worms or symptomatic immature infections are common. In cats, detectable antigenaemia develops at about 5.5 to eight months post-infection.

Antibody tests detect both male and female larvae as early as two months post-infection. However, antibody tests do not confirm current infection, simply that it has occurred. Studies indicate a wide range in sensitivity between antibody tests and limited evidence suggests that antibody levels decrease as the parasite matures.

The correct interpretation of serological tests requires care. Since both L5 larvae and adult worms can cause clinical disease in cats, the use of antibody and antigen tests in combination increases the likelihood of diagnosis.

Thoracic radiography, as in dogs, is valuable for assessing the severity of disease and monitoring its course. The characteristic pulmonary changes seen in infected cats are similar to those found in dogs. However, these may normalise and disappear completely, leaving no evidence of infection.

Ultrasonography is useful for identifying adult heartworms, particularly when several worms are present, and may confirm heartworm infection of at least five months’ duration.

Postmortem examination should include a careful search of the vena cavae, right side of the heart and pulmonary arteries. Special attention should be paid to the distal extremities of the pulmonary arteries. The systemic arteries, body cavities, brain and spinal canal should be examined thoroughly, as ectopic migration can occur.

Serologic retesting using both antibody and antigen tests at six to 12-month intervals is recommended for all infected cats. For asymptomatic cats, an annual retest may be adequate. Spontaneous or adulticide-induced elimination of infection in cats will generally result in the disappearance of detectable antigenaemia within four to five months. Cats that become antigennegative and clinically normal may continue to demonstrate positive antibody tests.

**Chemoprophylaxis and treatment in dogs**

Puppies in endemic areas should be started on chemoprophylaxis no later than eight weeks of age.
Early prophylaxis protects the individual and also reduces the reservoir population, resulting in a significant decrease in the prevalence of infection among unprotected dogs. Continuous chemoprophylaxis may not be necessary in areas with a distinct transmission season, but seasonal chemoprophylaxis may result in lowered compliance and lapses in protection if not given at appropriate times.

Macrocyclic lactones for monthly administration are available in oral (ivermectin, milbemycin oxime and moxidectin) and topical (selamectin) preparations. The US Food and Drug Administration has also approved a topical formulation of ivermectin combined with imidacloprid. A single subcutaneous injection of a slow release formulation of subcutaneously injected, moxidectin-impregnated lipid microspheres provides protection for at least six months.

Some collie dogs and other P-glycoprotein-deficient dogs are very sensitive to high doses of ivermectin and other macrocyclic lactones, but strict compliance with manufacturers’ instructions reduces the likelihood of adverse reactions in these dogs.

DEC is available in an oral form for daily dosing and is only protective when given continuously. A lapse of only two to three days may permit infection.

All adult dogs that may have been exposed to infection at least seven months prior to receiving chemoprophylaxis should be antigen-tested before treatment begins. Testing for microfilariae is mandatory before initiating or restarting prophylaxis with DEC.

If heartworm disease is confirmed, the dog’s clinical condition and the presence of co-existing diseases should be evaluated. The cardiopulmonary status is a good indicator of prognosis, as post-adulticide pulmonary thromboembolic complications occur most often in heavily infected dogs with signs of pulmonary arterial vascular obstruction and/or congestive heart failure.

Pulmonary thromboembolism is an inevitable consequence of effective adulticide therapy, and clinical signs include mild pyrexia, a cough, haemoptysis and right-sided heart failure. Signs may develop within seven to 10 days, but occasionally for as long as four weeks following treatment. Exercise restriction during the month following treatment reduces the likelihood of thromboembolic complications. Glucocorticosteroids can help control clinical signs of pulmonary thromboembolism, but studies evaluating their effect on the efficacy of adulticide therapy are lacking. Aspirin is not recommended.

A macrocyclic lactone should be given immediately after a positive diagnosis. This may reduce circulating microfilariae, kill migrating *D immitis* larvae, stunt immature *D immitis* and reduce female worm mass. The reduction in antigenic mass may then reduce the risk of pulmonary thromboembolism.

Close observation of higherrisk dogs is advised for the first eight to 12 hours following
administration of microfilaricidal drugs. Clinical signs associated with microfilariae death are generally mild, but severe cases require prompt treatment with intravenous fluids and glucocorticosteroids.

Melarsomine dihydrochloride is the most commonly used adulticide worldwide. It is administered via deep intramuscular injection into the epaxial lumbar muscles. Local reactions (such as soreness and swelling) are usually mild, provided the product is used according to the manufacturer’s recommendations. Clinically unwell dogs should be stabilised prior to adulticide therapy wherever possible. Exercise restriction during the recovery period is essential.

Treatment protocols vary depending on the disease’s severity. Dogs at a low risk of thromboembolisms are given two injections 24 hours apart. Those at a greater risk may benefit from a three-injection treatment protocol. These animals receive one dose initially and then a two-dose treatment four to six weeks later. The three-injection alternative protocol is the American Heartworm Society’s treatment of choice.

Since melarsomine does not kill immature worms (aged less than four months), three doses of a macrocyclic lactone (or an injection of slow release moxidectin) is recommended to kill pre-cardiac larvae, while allowing immature worms to mature and become susceptible to melarsomine.

An alternative treatment is to provide thiacetarsamide via two intravenous injections given eight hours apart on two consecutive days, for a total of four injections. Extravasation must be avoided or severe sloughing may result at, and adjacent to, the injection site. Caparsolate is also hepatotoxic and animals must be monitored carefully prior to each injection.

Continuous monthly administration of prophylactic ivermectin doses, alone or in combination with pyrantel pamoate, has been used as an alternative to arsenicals, with limited success. A course of prophylactic doses of ivermectin will gradually reduce the number of adult heartworms over one to two years, but this may be of limited benefit in chronic mature infections or in dogs with an active lifestyle.

Surgical extraction of worms is required in dogs displaying signs of caval syndrome. This develops acutely when large numbers of adult heartworms partially obstruct blood flow through the tricuspid valve, and is invariably fatal unless worms are surgically extracted.

A further indication for surgery is the presence of adult heartworms in the main pulmonary artery and lobar branches. Overall survival and rate of recovery by dogs at high risk of pulmonary thromboembolism is improved significantly by physically removing as many worms as possible before beginning adulticide therapy.

Heartworms may harbour obligate, intracellular and gramnegative bacteria belonging to the genus *Wolbachia*. Studies have shown that a surface protein induces a specific IgG response in hosts.
which may contribute to pulmonary and renal inflammation. Studies to determine the effects of suppressing *Wolbachia* populations with doxycycline prior to adulticide therapy are in progress.

Heartworm antigen testing is the most reliable method of confirming the efficacy of adulticide therapy and should be negative by six months post-treatment. If the animal remains antigen positive, repeat treatment may be considered, but is not always of further benefit in many dogs.

**Chemoprophylaxis and treatment in cats**

The benefit of heartworm prophylaxis in cats has been debated because of the species’ tendency to eliminate infection and the low incidence of disease, but most veterinarians recommend preventive therapy in endemic areas.

Heartworm chemoprophylaxis can be achieved with monthly doses of either oral (ivermectin or milbemycin oxime) or topical (moxidectin or selamectin) medications. Preventives should be started in kittens at eight weeks of age and be administered to all cats in heartworm-endemic areas during the heartworm transmission season.

Testing cats before initiating heartworm chemoprophylaxis is recommended, but not essential. Both an antigen and an antibody test should be performed, but testing for microfilariae is unnecessary. Testing confirms infection, aids the monitoring of infected cats, and establishes a baseline reference prior to initiating chemoprophylaxis.

If a cat tests positive for heartworm disease but displays no overt clinical signs, it is reasonable to allow time for a spontaneous cure to occur. The course of infection can be monitored periodically at six to 12-month intervals by repeat antibody and antigen testing, and thoracic radiography. Regression of radiographic signs and a negative antigen test are evidence that the infection has resolved. Antibody testing is of limited use in these cats.

Prednisone in tapering doses is often administered to infected cats with radiographic evidence of lung disease, regardless of whether the clinical signs are present. Glucocorticoids should also be given if antibody and/or antigen-positive cats display clinical signs. This treatment may be repeated in cats with recurrent clinical signs.

Cats that become acutely ill require aggressive supportive treatment in the form of intravenous corticosteroids and balanced electrolyte solutions, bronchodilators and oxygen. Diuretics, aspirin and NSAIDs are not indicated.

Adulticide administration is considered as a last resort for cats in stable condition, which are displaying clinical signs and are not controlled by corticosteroid therapy. Studies suggest that melarsomine is toxic at doses as low as 3.5mg/kg and it is not recommended for use in cats. Thiacetarsemide is not approved for use in cats.
Ivermectin given monthly over two years has been reported to reduce worm burdens by 65 per cent. However, since most cats have small worm burdens and may display an anaphylactictype reaction when the worms die, this form of treatment is of limited use.

To date, there is little evidence that any form of medical adulticidal therapy increases the survival rate of cats, and surgical removal is indicated in heavily infected or severely affected patients.

As in dogs, surgery is specifically indicated in those few cases that develop caval syndrome. The worms must be removed intact, since partial or complete traumatic transection of a worm may result in acute circulatory collapse and death.

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