Cornell Feline Health Center
Veterinary News
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Feline Heartworm Disease

Frank Smith, D.V.M.

Pet owners and veterinarians have long been aware of the problem of heartworms in dogs. Recently the problem is being recognized in cats. The increase in reported cases may be due to a heightened awareness of veterinarians to this problem in the cat; an increase in the number of necropsies performed each year; or a growing number of mosquitoes that will parasitize cats. Unfortunately for cats, this disease can be very difficult to diagnose and complications can be associated with the treatment of the disease.

The dog appears to be the natural host of the heartworm. Although cats do get the disease, they are much more resistant to infection than the dog and hence have fewer worms when infected. Studies have shown that 1-25% of third stage larva will mature to adults in cats, whereas 40-90% will mature to adults in dogs. The worms mature more slowly in the cat and the patency period is shorter. Microfilaremia is less common in the cat, being present in only 20% of the the heartworm-positive cats. Causes of amicrofilaremia include unisex infections, sterile females, immature females, ectopic infections, and removal of microfilaria by the reticuloendothelial system in the lungs. The heightened immune reaction in cats results in more severe pulmonary damage per worm in cats than in dogs. The adult heartworms live about two years in cats versus five years in dogs.

Pathology

Cardiopulmonary damage is common, secondary to heartworm infestations. The fifth stage larva can embolize the terminal branches of the pulmonary arteries resulting in a physical impediment to blood-flow. The presence of adults in the larger arteries causes endothelial damage which ultimately leads to villous proliferation of the intimal lining of the vessel wall. Muscular hypertrophy of the tunica media occurs in the smaller arteries. Damage to the vascular endothelium activates platelets and can initiate the coagulation cascade resulting in thrombus formation and subsequent infarction of the lungs. The allergic response to the heartworms results in a pulmonary infiltrate consisting predominantly of eosinophils. Many of these pulmonary changes result in narrowing of the vascular lumen which results in pulmonary hypertension, right ventricular hypertrophy and rarely right-sided heart failure. Several reports of neurological damage have been reported following aberrant parasite migration to the brain.

Clinical Disease

Any cat that is exposed to a mosquito runs the risk of developing heartworm disease. Cats ranging in age from 1-17 years have been reported with the disease. It is more commonly diagnosed in outdoor cats and male cats. This is probably due to their increased risk or exposure. There is no increased risk in cats with feline leukemia virus infections.

Cats with heartworms can be asymptomatic; they can have a sudden onset of severe signs; or they can have signs of chronic nature. The signs seen in an acute illness include collapse, dyspnea,

convulsions, vomiting, diarrhea, and blindness. It would be unlikely to see all these signs in one animal. Rarely will a seemingly healthy cat die suddenly, secondary to pulmonary thromboembolism. Cats with chronic illnesses caused by heartworms usually exhibit respiratory problems or vomiting. Rarely will the same animal exhibit both signs. Respiratory signs can include coughing, dyspnea, and hemoptysis. The coughing may wax and wane and often improves temporarily with steroid administration. The vomiting is usually sporadic. The vomitus is either food or foam and is rarely bile stained. Other signs of chronic disease include anorexia, lethargy, or neurologic abnormalities. Cats with chronic heartworm disease can still die acutely.

Diagnosis

The diagnostic process begins with a thorough physical examination. Most cats with heartworm disease have no physical abnormalities. Some cats will have harsh lung sounds while others may have cardiac arrythmias or murmurs.

The appropriate diagnostic tests will depend on the history and physical examination findings. The diagnostic plan for a chronically vomiting cat will obviously differ substantially from that for an acutely dyspneic cat. A complete blood count (CBC) will reveal a mild nonregenerative anemia and an eosinophilia in one-third of all heartworm-positive cats. The only common abnormality on a serum chemistry panel is a hypergammaglobulinemia. Urinalysis is usually normal.

Tests that are more diagnostic of heartworm disease include radiographs, electrocardiograms (ECG), echocardiograms (ECHO), a tracheal wash, a Knotts test, and serologic tests. Chest radiographs usually show enlargement and blunting of the pulmonary arteries which is best visualized in the caudal lobar arteries using the dorsoventral projection. The lung parenchyma may show atelectasis, perivascular infiltrates or an alveolar pattern. Sometimes the heart will be enlarged.

If the radiographs are suggestive of heartworm disease, an angiocardiogram may be performed. This technique clearly emphasizes the nature and extent of the pulmonary changes, the type of cardiac enlargement if present, and may outline adult heartworms in the pulmonary arteries. It can also be useful in ruling out cardiomyopathy as the cause of cardiomegaly.

To further evaluate the heart an electrocardiogram can be performed. With heartworm disease, it can be normal or it may confirm the presence of right heart enlargement. An echocardiogram can be useful in assessing cardiac function and characterizing cardiac changes. Heartworms are sometimes visualized with this technique.

If the physical examination and radiographs reveal pulmonary infiltrates a tracheal wash may be indicated. Inflammatory cytology is often seen, with eosinophils being the predominant cell type.

Cornell Feline Health Center
Veterinary News

A publication for veterinary professionals

The ultimate purpose of the Cornell Feline Health Center is to improve the health of cats everywhere, by developing methods to prevent or cure feline diseases, and by providing continuing education to veterinarians and cat owners. All contributions are tax-deductible.

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A definitive diagnose of the disease requires direct visualization of the microfilaria in the blood, detection of antibodies directed against the worms, or detection of adult cuticular antigens in the serum. A Knotts test is used to concentrate the microfilaria from a blood sample. However, because so many of the microfilaria are removed in the cats' lungs, only 20% of cats with heartworm disease will be diagnosed by this technique.

The most promising tests for the in-hospital diagnosis of heartworm disease in the cat are ELISA tests. The original test for heartworms measures antibodies in the serum directed against an adult cuticular antigen. This test is extremely sensitive, but false positive results do occur. A newer test detects the presence of an adult cuticular antigen in the serum of an infected animal. This test is equally sensitive, but has fewer false positive results.

Treatment

The treatment for cats is the same as for dogs. The adult worms are killed first very toxic to the kidneys and liver of the dog, but seems to be well tolerated by the cat. Although most cats can be treated sucessfully, some cats will experience complications resulting from the embolization of dead worms and thrombi. This can result in coughing, dyspnea, and hemoptysis. If the pulmonary damage is very severe, the cat may die. To minimize the risk of thromboembolism it is essential that the cat be strictly confined to a cage for 7-10 days after treatment, and be closely observed in a relatively confined environment for an additional 2-3 weeks.

Studies in the dog have shown that aspirin administration reduces pulmonary thromboembolism. Although its use in heartworm-positive cats has not been reported, it may be clinically useful. A safe dose would be 10 mg/kg every three days. Owners should be cautioned that treatment of the adult worms is not always 100% effective, and retreatment may be necessary. If microfilaria are present, as determined by a Knotts test, the cats are treated with either dithiazanine sodium or levamisole 4-6 weeks after the adults are killed. An ELISA test should be repeated 5-7 months after treatment to determine if all the adults have been killed. Cats can be treated with diethylcarbamazine to prevent heartworm infection. This decision should be based on the incidence of heartworms in your area.

Although heartworm disease in the cat is still an uncommon disease, it should be considered in cats with a history of chronic vomiting or respiratory problems.■

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Frank Smith received his D.V.M. degree from Cornell University (1983) and completed his internship in 1984. He is beginning his second year as a resident in small animal internal medicine.

Explanation of FeLV

Gary Cockerell,

Since the spring 1985 issue of "Veterinary News", which contained guidelines for the use of Norden Laboratories' new feline leukemia vaccine (Leukocell®), the Cornell Feline Health Center has received numerous requests for additional information. Expanded below are the policy guidelines for use of Leukocell® in the Veterinary Medical Teaching Hospital at Cornell University, addressing the most frequently asked questions.

1. "Before vaccination or at the time of vaccination the cat should be tested for the feline leukemia virus."

We are more firm in this recommendation than Norden Labs. If a vaccinated cat of unknown FeLV status at the time of vaccination is subsequently found to be FeLV-positive, it would be impossible to determine whether the cat was viremic prior to vaccination, the vaccine induced the viremia, or the vaccine failed to prevent infection by FeLV exposure after vaccination.

We suggest the ELISA as a prevaccination screening test for FeLV because it can detect cats in the incubation period of the infection prior to the bone marrow stage of infection and a positive immunofluorescent test (IFAT). The ELISA will also pick up those "test-discordant" cats which remain persistently ELISA-positive but IFAT-negative. We consider a positive result on either test to indicate viremia, in which case vaccination is of no benefit. Ideally, the test should be done prior to the first vaccination. This saves the expense of a separate office visit simply for the purpose of the prevaccination test. Several ELISA kits now enable results to be obtained within one-half hour, and a decision as to whether or not to vaccinate can be made during the same visit.

ELISA test occasionally can give false positive reactions due to operator error or slight non-specific reactions. ELISA-positive cats should always be rechecked in 3-4 weeks, and in our opinion, persistently ELISA-positive cats should be tested by the IFA test before they are condemned.

2. "Cats which have the greatest potential for infection should be vaccinated (e.g. show cats, shelter cats, negative cats going into multiple households, outdoor cats)."

The purpose of this guideline is to reserve vaccination for those cats with the highest risk of exposure to FeLV, rather than to employ Leukocell® as a standard immunization similar to vaccines which provide protection against other common, but more easily transmitted feline infectious diseases. FeLV is not an efficiently transmitted agent, but rather requires prolonged and close contact for its spread from infected to uninfected cats. Therefore, for single or even small groups of FeLV-negative cats which are maintained in isolation from other possibly FeLV-positive cats, the risk of FeLV-infection is negligible. On the other hand, we never can predict when a FeLV-positive stray cat will adopt one of these isolated, single cat households. Certainly, vaccination under these conditions can do no harm, but probably it is an unwise expenditure of the client's money.

3. "A series of three intramuscular injections should be given in the following intervals: 9 weeks or older; 3 weeks later; and 3 months later. Thereafter, an annual booster to maintain immunity."

Vaccine Guidelines

D.V.M., Ph.D.

This recommendation is strictly in accordance with the vaccination "windows" given by Norden, but is somewhat more specified so as to be in synchrony with the primary immunization schedule at the VMTH against other feline pathogens. Norden indicates that simultaneous use of Leukocell® with other established feline vaccines and immunization regimens does not interfere with the resultant immune response. Cats become more resistant to FeLV infection with age, but annual booster vaccination for the life of the cat.

> **4. "If the initial blood test is positive do not vaccinate or discontinue the vaccination program and retest in one month. Also do not vaccinate cats that are pregnant or blood donors."**

Any cat that remains FeLV-positive with repeated tests conducted at 1 to 3 month intervals should not be vaccinated, but considered persistently viremic and handled accordingly. The recommendation not to vaccinate pregnant queens is based upon general principles of immunization rather than specific concern related to Leukocell®.

The recommendation not to vaccinate blood donors is based totally on present theoretical considerations. Since Leukocell® is prepared from antigenic material shed from a FeLV-infected feline lymphoblastoid cell line in tissue culture, it is possible that feline histocompatibility anitgens might be present in the vaccine. Immunization with these antigens might therefore induce allogeneic immune reactivity (or perhaps even be partially responsible for some of the adverse reactions observed during the primary immunization regimen) which could be transferred in the blood of a vaccinated donor cat to a recipient cat. Until this possibility has been investigated it seems more prudent to protect blood donors from FeLV by strict isolation and to reconfirm their FeLV-negative status by repeated testing, rather than by vaccination.

> **5. "If the second test is negative the cat has experienced a transient viremia and may now be naturally immune; however, vaccination should in initiated or resumed to further booster immunity."**

Under natural conditions, many FeLV-exposed cats experience a transient viremia followed by an immune response that eliminates viremia, the cat reverts to FeLV-negative status and is thought to be FeLV-immune. However, since the actual anti-FeLV or anti-FOCMA antibody titers in these cats are seldom known, it seems most prudent to proceed with immunization and boost whatever naturally acquired immunity may be present.

> **6. "If the second FeLV test is positive, the cat is persistently viremic and should be handled accordingly. Vaccination of positive cats has no detrimental or beneficial effects."**

There is no evidence that Leukocell® can reverse an established FeLV viremia, or alter the clinical course in viremic cats. Neither is there evidence that the vaccine produces any greater untoward effects in FeLV-positive than FeLV-negative cats, but it is wasteful of client's money. Also it may be embarassing to veterinarians if owners are not properly informed and a FeLV-positive cat develops a FeLV-related disease subsequent to vaccination.

Other Considerations

Leukocell® is a promising first generation vaccine which provides for the first time the possibility of preventing FeLV infec-

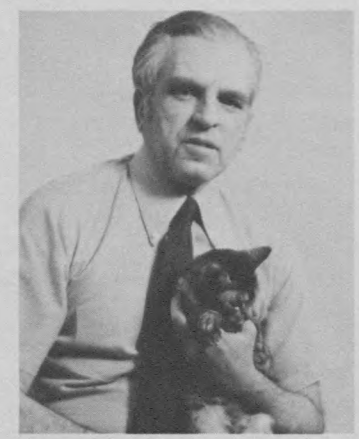
tion by any practical means other than environmental isolation of susceptible cats. Approximately 80% of vaccinated cats remained healthy after an experimental challenge with a large dose of virulent FeLV in conjunction with corticosteroid-induced immunosuppression. Protection, therefore, is not complete. This is a more severe challenge than cats experience under natural conditions, but this does not necessarily equate with an expected greater rate of protection in the field where cats are exposed to multiple small doses of the virus in association with other environmental factors. This information will be forthcoming in the next several years as results from the use of the vaccine in natural exposure environments become available.

The ability of Leukocell® to prevent latent FeLV-negative infections or the effect of vaccinating latently infected cats are unknown. Furthermore, the actual clinical significance of latent FeLV infection remains incompletely understood. Latent FeLV infections are not detected by routine ELISA or IFAT procedures and therefore it is certain that some FeLV-negative, but latently FeLV-infected cats, will be vaccinated.

The vaccine itself will not produce a FeLV-positive test, nor does it contain infectious FeLV. As reported by Norden Laboratories, Leukocell® does produce adverse reactions in about 13% of vaccines. Reactions mostly include local pain and discomfort at the vaccination site, but also occasional transient systemic reactions such as lethargy, fever, anorexia and diarrhea. Reports from veterinarians indicate that serious, transient adverse reactions occur in less than 1% of vaccinated cats, and therefore the clinican must be ready to treat these cats promptly as indicated. Norden Laboratories are attempting to identify the cause of these reactions, and have test kits that they will make available to veterinarians to skin test reactor cats. If you are interested in pursuing the cause of the adverse systemic reaction in a cat following Leukocell® vaccination, call Norden Laboratories, (402) 475-4541.

Finally, while Leukocell® provides a useful aid in reducing the incidence of FeLV infection in cats, its use should not provide a false sense of security. Protection is not absolute. Vaccination should add to, but not replace, existing test and removal or isolation programs for FeLV-infected cats.■

Dr. Robert Kirk Retires



Dr. Robert W. Kirk will retire on July 12 from the faculty of the New York State College of Veterinary Medicine at Cornell University. He has held positions as professor and chairman of small animal medicine, and director of the Veterinary Medical Teaching Hospital. He is the author or editor of several books, including the world-famous Current Veterinary Therapy.

Dr. Kirk has been a participant of the Cornell Feline Health Center since its founding in 1974. His encouragement and support have been greatly appreciated.

A retirement celebration will be held on Sunday, July 14 at 5 pm. For information and reservations contact:

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If you would like to contribute material for a memorabilia book for Dr. and Mrs. Kirk, please send items to the above address.■

Toxoplasmosis: Interpretation of Serological Results

Richard H. Jacobson, M.S., Ph.D.

Based on many telephone conversations with practitioners, we find that interpretation of serological results for toxoplasmosis is poorly understood in terms of its relationship to the differential diagnosis and its zoonotic implications. This apparently results from a misunderstanding of the disease in cats and its epidemiological implications.

A positive serological result in cats simply means that the cat has been previously infected with the agent, Toxoplasma gondii. In the absence of clinical manifestations suggestive of toxoplasmosis, it has little significance in disease diagnosis. Although there is a relatively high prevalence rate of this infection in cat populations, overt clinical disease associated with it is fairly uncommon. The parasite is very well adapted to its host and often can remain viable in the host's tissues for years without causing clinical signs.

Indoor cats generally are serologically negative unless they are habitually fed raw meat products. Outdoor cats, including those which are allowed outside for brief intervals, have the highest prevalence rates of toxoplasmosis. Following ingestion of an infectious meal, oocyst production begins in several days and continues for 14-21 days with millions of oocysts being shed in the feces. After this period, oocyst shedding usually ceases commensurate with the appearance of serum antibody. Generally, however, the cat does not shed oocysts after its immune response is activated. Therefore, even though a cat may be serologically positive for extended periods, it generally will not be shedding oocysts.

Recrudescence of oocyst shedding is relatively uncommon. It has been experimentally induced, although at substantially reduced levels and for abbreviated intervals, following immunosuppressive therapy or subsequent to immunosuppressive infections. If a serologically positive cat ingests another infectious meal, oocyst shedding is generally not observed. If in the rare event it does occur, only a few oocysts are shed for a short time.

Elevated antibody levels in chronically infected cats are usually persistent. When the differential diagnosis for a clinically ill cat includes toxoplasmosis and the cat is serologically positive for toxoplasmosis, clincians often conclude that toxo is the problem. Usually T. gondii is not very pathogenic in cats. It is highly prevalent in some cat populations, and may have been present in the cat a long time prior to the current condition. Hence, the current titer may be incidental to the clinical observations.

Alternatively, a positive toxo titer may indeed support the clinical findings, particularly when the titer is very high. This is suggestive of increased stimulation of the immune system either by a recently acquired infection or by the persistent release of zoites from the pseudocysts in tissues harboring large numbers of organisms. Periodically, however, we see high titered cats which are clinically normal. Therefore, the level of anti-toxo antibody in cats is not necessarily directly related to disease.

Test Kits

Recently, test kits for detecting antibody to T. gondii in the cat's serum have become available. Generally, these only indicate whether the cat is serologically positive or negative (qualitative result)

and do not provide a titer (quantitative result). If one is screening cats for the presence of anti-toxo antibody, possibly to assess the infection status of the cat for a client, then the tests can provide useful information. These results can be misleading when confirming a clinical diagnosis of toxoplasmosis. A positive test may be due to antibody production from previous exposure, but is unrelated to the current problem. The serological confirmation of clinical toxoplasmosis in cats requires quantitative results on paired samples.

With the current increase in serological testing systems it is essential that clinicians demand an interpretation of serological results for a given system. This is especially important because there are no officially accepted standards for test validation. Only when interpretative information includes many of the aforementioned factors, then an informed interpretation can be made which will lend support to the differential diagnosis.

Conclusion

A serologically positive cat generally is not shedding oocysts and rarely would be a source of infection to humans. Under certain immunosuppressive conditions, oocysts may appear in the feces. Therefore, we recommend that pregnant women take precautions when handling cat litter pans, even though transmission is remote.

Don't overinterpret a positive serological result in which toxoplasmosis is included in the differential diagnosis. Remember, cats with chronic T. gondii infection may have positive titers for years even though no clinical manifestations of the disease may be evident. Thus, titers in clinically ill animals may be irrelevant in the differential diagnosis.

Quantitative results are the most useful in assessing the significance of serology for toxoplasmosis. Although some useful information can be obtained from qualitative tests, their usefulness in understanding the role of T. gondii in a differential diagnosis is reduced due to the relatively high prevalence of the infection in certain cat populations. ■

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