

# Causes of endogenous uveitis in cats presented to referral clinics in North Carolina

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## Abstract

**Objective** To investigate the causes of endogenous uveitis in cats presenting to referral ophthalmology clinics in North Carolina.

**Procedure** Medical records of cats diagnosed with endogenous uveitis at North Carolina State University's College of Veterinary Medicine (NCSU-CVM) or Animal Eye Care Associates of Cary, NC between 2003 and 2015 were reviewed. Inclusion criteria were cats that had complete diagnostic workups, including clinical, clinicopathological, serological, and histopathological data, as well as imaging modalities. Serology was consistently completed for feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline coronavirus (FCoV), *Toxoplasma gondii*, and *Bartonella* spp.

**Results** One hundred and twenty cats met the inclusion criteria. Seroprevalence of FeLV (2.7%), FIV (7.3%), FCoV (34.7%), *T. gondii* (23.7%), and *Bartonella* spp. (43.2%) was observed, with a combined seroprevalence of 59.2%. Nineteen cats (15.8%) were diagnosed with feline infectious peritonitis (FIP) based on clinical, hematological, serological, histopathological, and necropsy findings. The average age of all cases was 7.62 years, while the average age of cats diagnosed with FIP was 1.82 years. Neoplasia was diagnosed in six cats (5.0%). No underlying etiology was found in 49 cats (40.8%).

**Conclusions** Both idiopathic and neoplastic causes of uveitis were less prevalent than previously reported in studies, while seropositivity was higher than previously reported for the study area. This may be due to improved diagnostic capabilities or that cats with infectious disease were more likely to be referred. Because of the high prevalence of FIP, young cats with uveitis should be evaluated for hyperglobulinemia and FCoV serology should be performed as minimal diagnostics.

**Key Words:** causes, endogenous uveitis, feline uveitis, prevalence

## INTRODUCTION

Feline uveitis, which is a common ocular condition, is usually divided into exogenous and endogenous causes.<sup>1</sup> Exogenous causes are commonly identified by a thorough ocular examination and include trauma, corneal ulcers, and lens luxations. Endogenous causes, which are the most common cause of uveitis in cats, tend to be divided into large categories, including infectious, neoplastic, and immune-mediated or idiopathic.<sup>2</sup> The most commonly reported infectious agents associated with feline endogenous uveitis are feline leukemia virus (FeLV),<sup>3,4</sup> feline immunodeficiency virus (FIV),<sup>5,6</sup> feline coronavirus (FCoV) causing feline infectious peritonitis (FIP),<sup>4,7</sup> bartonellosis,<sup>8,9</sup> toxoplasmosis,<sup>10,11</sup> and systemic fungal

infections, including cryptococcosis,<sup>12,13</sup> histoplasmosis,<sup>14</sup> blastomycosis,<sup>15</sup> and coccidioidomycosis.<sup>16,17</sup> The most common primary neoplastic cause of uveitis is iris melanoma, followed by trauma associated sarcoma, while the most common metastatic neoplasia is lymphoma.<sup>2,18</sup>

Determining the specific etiologic agent causing uveitis can be difficult due to a similar clinical presentation of most endogenous causes. While neoplasia may be diagnosed based on appearance and confirmed with cytology of aqueous humor or biopsies, aqueous humor cytology is generally not as beneficial in definitively diagnosing infectious agents.<sup>19</sup> Therefore, a thorough physical examination, complete blood cell count, serum biochemistry profile, urinalysis, thoracic radiographs, abdominal ultrasound, and select serological titers are recommended in

many cases of endogenous uveitis to narrow down the differential list.<sup>20</sup> In addition, despite their inability to definitively diagnose the cause of endogenous uveitis, aqueous humor serology and polymerase chain reaction (PCR) are still methods used to investigate possible causes, including *Bartonella* spp, *T. gondii*, FCoV, and feline herpesvirus-1 (FHV-1). Aqueous humor serology and PCR results, as well as serum serology, must be interpreted carefully, as serology usually indicates exposure, not active infection, and the high sensitivity of PCR can make it difficult to determine whether an infection is active.<sup>21</sup>

Retrospective studies investigating the causes of feline uveitis were completed in the early 1990s, and diagnoses relied heavily on results of serologic tests<sup>22–24</sup> or histopathology.<sup>4</sup> These studies found that between 16–20%<sup>23,24</sup> and 70%<sup>22</sup> of cases had no evidence of a systemic cause or infection. A more recent study investigating the diagnostic quality of aqueous humor serology, found similar results, in that 40% of cats with uveitis had serum that was serologically negative for FeLV, FIV, *Toxoplasma*, and *Bartonella* spp.<sup>21</sup> One study published in 1991, that focused specifically on cats presenting to ophthalmologists in North Carolina, found infectious agents caused 15% of uveitis cases, neoplasia caused 13%, and systemic hypertension caused 2%. The remaining 70% of cases were deemed idiopathic.<sup>22</sup> With the advance of new diagnostic tests and a greater awareness of possible etiologic agents, the purpose of this study was to investigate the causes of feline endogenous uveitis in North Carolina by reviewing the medical records of cats diagnosed with endogenous uveitis at referral ophthalmology clinics in North Carolina.

## MATERIALS AND METHODS

Medical records of cats that were presented to the Ophthalmology Service at the NCSU-CVM or Animal Eye Care Associates of Cary, North Carolina, between 2003 and 2015 were reviewed. To be included in the study, patients were required to be diagnosed with endogenous uveitis by a board certified veterinary ophthalmologist and have had serological/PCR testing for at least three of the five diseases in focus (FeLV, FIV, FCoV, *Bartonella* spp, and *T. gondii*), or a definitive diagnosis based on cytology or histopathology. Additional supportive diagnostic tests performed on an individual case basis were recorded and included complete blood cell counts, serum chemistry analysis, urinalysis, thoracic radiographs, abdominal ultrasound, CT scan, cytology, and additional serologic or PCR tests for fungal and vector borne diseases. Patients' signalment, laterality of the affected eye, duration of clinical signs, and when available, outcome, were recorded.

## RESULTS

A total of 120 cats were included in this study, with a mean age of 7.62 years (median age 8.05 years), ranging

from 6.5 weeks to 19 years. The male to female ratio was 1.66:1 (75 males, 45 females). Domestic short-hair cats were overly represented (89), followed by domestic long-hair cats (nine), domestic medium-hair cats (five) and Siamese (four), or Siamese mixes (three). Himalayan (three), Bengal (two), Sphynx (one), Manx (one), Egyptian Mau (one), Siberian (one), and Maine Coon (one) breeds were also represented. A total of 43 cats presented with bilateral uveitis, while 77 cats had unilateral uveitis. Complete blood cell counts were completed on 103 patients, serum chemistry analysis was completed on 106 patients, and urinalyses were completed on 27 patients.

A total of 34 cases from the NCSU-CVM were included in this study. Various commercial and in-house protocols were used to test for infectious agents. Commercial kits (SNAP FIV/FeLV Combo Test from Idexx Laboratories Westbrook, Maine) were used for the detection of FeLV antigen and FIV antibodies (32 cats). FCoV PCR (10 cats) was completed using a procedure previously described<sup>25</sup> by the NCSU Clinical Virology Diagnostic Laboratory, which also completed serological testing using an immunofluorescent antibody test (IFA) (14 cats) for FCoV. Serum was assayed for IgM and IgG *T. gondii* antibodies (26 cats) through the Veterinary Diagnostic Laboratory at Colorado State University using a previously described procedure.<sup>26</sup> Cats were tested for *Bartonella* spp. using a variety of tests through the Vector Borne Disease Diagnostic Laboratory at North Carolina State University, including culture (1 cat), culture with PCR (3 cats), and PCR alone (1 cat) using a procedure outlined in Duncan *et al.*<sup>27</sup> In addition, PCR and serology was performed using an IFA procedure from Hegarty *et al.*,<sup>28</sup> but modified by the use of goat antifeline conjugated IgG, substituted for anticanine conjugated IgG, for *B. henselae*, *B. vinsonii*, and *B. koehlerae* (1 cat), or *B. henselae* alone (2 cats).

A total of 86 cases from Animal Eye Care of Cary, North Carolina, were included. The majority of bloodwork was completed by Antech Diagnostics (Irvine, CA), including an enzyme-linked immunosorbent assay (ELISA) test for FeLV antigen and FIV antibody (70 cats), an IFA for FCoV antibodies (70 cats), and *T. gondii* antibody titers for IgM and IgG (64 cats). A variety of tests were completed for *Bartonella* spp., including an IFA for *B. henselae* (25 cats) and PCR for *B. henselae*, *B. clarridgeiae*, and *B. quintana* (2 cats) by Antech Diagnostics. In addition, PCR, culture and serology (IFA) for *B. henselae* and *B. vinsonii* (4 cats), PCR (2 cats), and IFA for *B. henselae* (1 cat) were completed by the Vector Borne Disease Diagnostic Laboratory at NCSU using the same procedures cited previously.<sup>27, 28</sup> Additional diagnostic tests were completed by other laboratories including an ELISA for FeLV antigen and FIV antibody (3 cats), FCoV IFA (2 cats), and *T. gondii* IgM and IgG antibody titers (2 cats) by Idexx Laboratories (Westbrook, ME), and *Bartonella* spp. PCR (1 cat) by Galaxy Diagnostics (Morrisville, NC). Finally, nine cats had a combination of test results for

FeLV, FIV, FCoV, *T. gondii*, *Bartonella* spp., and *Cryptococcus* reported prior to referral and the laboratory performing these tests was not recorded.

Serological testing for infectious agents was performed in all but five patients. Those cats that did not have diagnostic testing for infectious agents were diagnosed with neoplasia based on cytology and histopathology. In total, 61.7% of the patients tested for infectious disease (and 59.2% of all patient) were either serologically or PCR positive for FeLV, FIV, FCoV, *T. gondii*, *Bartonella* spp., *Cryptococcus neoformans*, or a combination of these agents. However, not all patients were tested for every agent, as shown in Table 1. Of the patients tested for FeLV and FIV, 2.7% and 7.3%, respectively, were serologically positive for these viruses. Seropositivity for those cats tested for *T. gondii* was 23.7% as shown in Table 2. Using a combination of serology, culture, and PCR to test for *Bartonella* spp., 43.2% of those patients tested had positive results. All of the cats with positive results were seropositive for *B. henselae*, as shown in Table 3. Of the 42 patients tested for both *T. gondii* and *Bartonella* spp., five were serologically positive for both agents. In addition to these five etiologic agents, nine cats were tested for fungal agents, including blastomycosis, histoplasmosis, aspergillosis, cryptococcosis, and coccidioidomycosis. One cat was positive for *Cryptococcus* antigen.

Of the 115 cats that underwent diagnostic testing for infectious agents, 44 (36.6%) were negative for all agents for which they were tested. However, one of these patients was diagnosed with lymphoma, and five were ultimately diagnosed with FIP. The remaining 38 cases (31.7%) were deemed to be idiopathic, as they were clear of all systemic diseases for which they were tested. However, only seventeen (14.2% of the total 120 cases) were tested and

**Table 1.** Serological or PCR presence of feline leukemia virus, feline immunodeficiency virus, feline coronavirus, *Toxoplasma gondii*, *Bartonella* spp., and *Cryptococcus neoformans* in 120 cats with endogenous uveitis

Infectious Agent	Number Positive	Number Tested	% Positive
Feline leukemia virus	3	112	2.7%
Feline immunodeficiency virus	8	109	7.3%
Feline coronavirus	34	98	34.7%
PCR	3	10*	
Serology	31	89	
<i>Toxoplasma gondii</i>	22	93	23.7%
<i>Bartonella</i> spp.	19	44	43.2%
<i>Toxoplasma gondii</i> and <i>Bartonella</i> spp.	5	42	11.9%
<i>Cryptococcus neoformans</i>	1	8	12.5%
Total Seropositivity/ PCR positivity	71	115	61.7% (59.2% of total cases)

\*1 test was combined PCR and Serology

negative for all five infectious agents. The infectious disease tests that were not performed for cases clinically diagnosed with idiopathic uveitis can be found in Table 4. In addition to these cases, there were eleven cases diagnosed with idiopathic uveitis, despite having a positive serological titer for FCoV, due to the fact that their other clinical signs and bloodwork values were not consistent with a diagnosis of FIP. Therefore, a total of 49 cases (40.8%) were deemed idiopathic, despite some cases having positive test results for FCoV. While this distinction was made for cats with FCoV, this was not carried out for *T. gondii* and *Bartonella* spp. seropositivity, due to the difficulty of interpreting serology for these agents. The average age of these 49 idiopathic cases was 8.60 years, and the male to female ratio was 1.72:1.

**Table 2.** Serological test results for *Toxoplasma gondii*

Titer	Number (% of those tested) 93 cats in total
Negative titer	71 (76.3%)
IgM 1:64	3 (3.2%)
IgM 1:64, IgG 1:256	1 (1.1%)
IgM 1:64, IgG 1:1024; 1 month later IgG 1:512	1 (1.1%)
IgG 1:64	1 (1.1%)
IgG 1:128	5 (5.4%)
IgG 1:256	2 (2.2%)
IgG 1:512	3 (3.2%)
IgG 1:512, 1 month later 1:1024	1 (1.1%)
IgG 1:1024	2 (2.2%)
IgG 1:2048	1 (1.1%)
IgG 1:4096	1 (1.1%)
IgG 1:4096; 3 months later 1:1024	1 (1.1%)
Total Seropositivity	22 (23.7%)

**Table 3.** Diagnostic test results for *Bartonella* spp.

Titer/PCR Results	Number (% of those tested) 44 cats in total
Negative (PCR and IFA for <i>B. henselae</i> , <i>B. vinsonii</i> , <i>B. koehlerae</i> )	1 (2.3%)
Negative (PCR, culture, and IFA for <i>B. henselae</i> , <i>B. vinsonii</i> , <i>B. koehlerae</i> )	4 (9.1%)
Negative (IFA for <i>B. henselae</i> )	10 (22.7%)
Negative (Culture)	1 (2.3%)
Negative (PCR)	6 (13.6%)
Negative (PCR and culture)	3 (6.8%)
Total number of cats with negative results	25 (56.8%)
<i>B. henselae</i> IgG 1:64	5 (11.4%)
<i>B. henselae</i> IgG 1:128	4 (9.1%)
<i>B. henselae</i> IgG 1:128, 5 months later 1:1024	1 (2.3%)
<i>B. henselae</i> IgG 1:256	4 (9.1%)
<i>B. henselae</i> IgG 1:512	3 (6.8%)
<i>B. henselae</i> IgG 1:2000	1 (2.3%)
<i>B. henselae</i> IgG 1:4096	1 (2.3%)
Total Seropositivity	19 (43.2%)

**Table 4.** Classification of the infectious disease tests missing for each of the 49 cats diagnosed with idiopathic uveitis

Missing tests	Number of cats	Number of feline coronavirus seropositive cats, in which FIP was excluded as a possible cause	Total number of cats diagnosed with idiopathic uveitis
Complete testing for all 5 agents (FeLV, FIV, FCoV, <i>T. gondii</i> , and <i>Bartonella</i> spp.)	12	5	17
Missing <i>Bartonella</i> spp.	22	4	26
Missing <i>T. gondii</i>	0	1	1
Missing feline coronavirus and <i>Bartonella</i> spp.	2	0	2
Missing <i>T. gondii</i> and <i>Bartonella</i> spp.	2	1	3
Total	38	11	49

While 34.7% (34 of the 98 patients tested, as shown in Table 5) of cases tested for FCoV had serological or PCR evidence of infection with FCoV, only nineteen cats (15.8%) from the total 120 cases were diagnosed with FIP. Ten cats were diagnosed based on histopathology, while the other nine were diagnosed based on serology, signalment, bloodwork, clinical signs, imaging, necropsy, and the clinical course of each patient. The average age of cats diagnosed with FIP was 1.82 years. The male to female ratio was 1.72:1.

Six patients (5.0% of all cases) were diagnosed with neoplasia. The average age of these patients was 11.1 years, and the male to female ratio was 1:1. Only one case was primary neoplasia, diagnosed with histopathology as diffuse iris melanoma. The other five cases were either metastatic lymphoma (3 cats, 2.5% of all cases), diagnosed

based on cytology of abdominal fluid and lymph node aspirates, or metastatic adenocarcinoma (2 cats, 1.7% of all cases), diagnosed based on ocular histopathology.

In addition to these six neoplastic cases, 31 other cases, for a total of 37 cases (30.8%), were diagnosed with a definitive cause of uveitis, including FIP, cryptococcosis, FIV, and FeLV, as shown in Table 6.

## DISCUSSION

This study demonstrates that the prevalence of the most common causes of feline endogenous uveitis in North Carolina has varied over time, and the data presented can provide valuable information for practicing veterinarians. In this study, 40.8% of cases were considered idiopathic and a definitive diagnosis was found in 30.8% of cases (37 cats), including neoplasia, FeLV, FIV, FIP, and cryptococcosis. FIP was most commonly diagnosed at 15.8%, while neoplasia was only diagnosed in 5.0% of cases. Although serological results for toxoplasmosis and bartonellosis can be difficult to interpret, in total only 29.2% (35 cases) of patients were seropositive for either *Bartonella* spp. or *T. gondii*. While these data provide information to help guide the diagnostic process, it is important to note that given the retrospective nature of this study, some factors must be addressed.

A limitation of this study is that not all patients were consistently tested for every infectious agent. This makes drawing conclusions about the actual total number of idiopathic cases difficult, and it is likely this study overestimated the number of disease free cats. In addition, various diagnostic tests with variable sensitivities and specificities were completed for each specific infectious agent. Again, this may have influenced the number of systemic diseases reported, but likely is a more realistic representation of a clinical setting, as some patients will have had serological testing prior to referral. Finally, in most

**Table 5.** Diagnostic test results for feline coronavirus

Titer/PCR	Number (% of those tested) 98 cats in total
Negative (Serology)	57 (58.2%)
Negative (PCR)	6 (6.1%)
Negative (PCR and serology)	1 (1.0%)
Total number of cats with negative results	64 (65.3%)
Positive (Titer > 1:400 and 1:1600)	13 (13.3%)
Positive (Titer 1:6400)	1 (1.0%)
Positive (PCR)	3 (3.1%)
Weak Positive (Titer >1:400, <1:1600)	12 (12.2%)
Weak Positive (Titer <1:400)	5 (5.1%)
Total number of cats with positive results	34 (34.7%)
Total number of cats with titers >1:1600, or PCR positive results	17 (17.3%)

**Table 6.** Classification of the definitively diagnosed causes of feline uveitis in 120 cats with endogenous uveitis

Cause	Number of cases (% of total)
Neoplasia	6 (5.0%)
Primary	
Iris Melanoma	1 (0.8%)
Secondary	
Lymphoma	3 (2.5%)
Metastatic Adenocarcinoma	2 (1.7%)
Feline leukemia virus	3 of 112 (2.7% of those tested)
Feline immunodeficiency virus	8 of 109 (7.3% of those tested)
Feline infectious peritonitis	19 (15.8%)
<i>Cryptococcus neoformans</i>	1 of 8 (12.5% of those tested, 0.8% total)
Total cases with a definitive diagnosis	37 (30.8%)

instances, serology was the only diagnostic performed to test for *T. gondii* and *Bartonella* spp., while histopathology, bacterial cultures, and PCR were more rarely completed. Interpreting the clinical significance of seropositivity for *T. gondii* and *Bartonella* spp. is difficult. While many cases did have a definitive diagnosis, toxoplasmosis and bartonellosis cannot be diagnosed as causes of uveitis based solely on the presence of seropositivity.<sup>10,11,21,29,30</sup>

In addition, there are no pathognomonic ocular lesions for bartonellosis or toxoplasmosis. Toxoplasmosis can only be definitively diagnosed with histopathology.<sup>31</sup> However, while organisms are commonly found in the eyes in patients with disseminated toxoplasmosis, it is rare to find the organism in the eyes of cats whose only manifestation of *T. gondii* is ocular disease.<sup>4,29</sup> In addition, while studies have found that PCR<sup>32,33</sup> and serology<sup>10</sup> for *T. gondii* reveal positive results when performed on the aqueous humor of cats with uveitis, these same studies also found positive results in the eyes of clinically normal cats. This makes diagnosing *T. gondii* as the cause of uveitis in patients with only ocular disease very difficult. While serology cannot definitively diagnose an active toxoplasmosis infection due to the fact that IgG titers can remain elevated for two years or longer following infection,<sup>34</sup> a fourfold rise in IgG titers over two to five weeks, or an IgM titer greater than 1:64 has been associated with active toxoplasmosis infections.<sup>35</sup> If these factors were used to evaluate the *T. gondii* titers of the cats in this study, it would indicate that there were no cases of uveitis caused by active *T. gondii* infections, although only three animals had paired titers (see Table 2).

In a population setting, however, serological testing can still be beneficial to investigate the prevalence of *T. gondii*. Worldwide, the estimated seroprevalence of *T. gondii* is 30–40%,<sup>36,37</sup> but this varies with location, as it has been reported as high as 97% in Egypt.<sup>38</sup> Seroprevalence within the United States ranges from 8 to 80%.<sup>39</sup> The seropositivity specifically in cats with uveitis has been documented to be between 74 and 78%, which is considerably higher than the seroprevalence in healthy cats in those same areas at 42.9% and 49.4%.<sup>10,23</sup> The total seroprevalence of *T. gondii* in patients included in this study was lower at only 23.7%. This is consistent with more recent studies, in which 18.3% of cats with uveitis were seropositive in a nation-wide study performed in 2010,<sup>21</sup> and 34% of healthy cats were found to be seropositive in a nearby geographic area of this present study in Randolph County, North Carolina.<sup>40</sup>

Similar to *T. gondii*, it can be difficult to diagnose bartonellosis as the causative agent of uveitis. The gold standard for diagnosing bartonellosis is isolation of the bacteria, but even this is nonconfirmatory as healthy cats in endemic areas can be bacteremic.<sup>41</sup> Like *T. gondii*, using aqueous humor for PCR or serology can help strengthen a presumed diagnosis of bartonellosis, but cannot be used for definitive diagnosis.<sup>9,21</sup> Serology must be interpreted

very carefully, as previous studies have documented a higher seroprevalence for *Bartonella* spp. in healthy cats, than those with uveitis.<sup>21,30</sup> Although this could be due to the high flea prevalence of the healthy cats included in these studies, a recent study from 2010 also found that there was no association between feline patients with uveitis and seropositivity for *Bartonella* spp.<sup>42</sup> Therefore, like *T. gondii*, serology for *Bartonella* spp. can be helpful to rule out bartonellosis, as its negative predictive value is 89–97%; however, it is not very helpful in diagnosing the cause of uveitis in individual cases.<sup>43</sup>

On a population level, *Bartonella* spp. seroprevalence can still reveal valuable information. Like *T. gondii*, seroprevalence for *Bartonella* spp. varies with geography, and additionally, it is associated with flea populations.<sup>44</sup> In general, seroprevalence can range from 10 to 80% in apparently healthy cats,<sup>43</sup> and a study completed in Randolph County, North Carolina, found 75% of healthy cats were seropositive for *B. henselae*.<sup>40</sup> This present study, which was completed in a similar geographic area to that study, found *Bartonella* spp. seroprevalence for cats diagnosed with uveitis was only 43.2%. Not only is this lower than previously reported for this study area, this value is also lower than values from previous studies of cats with uveitis, which range from 53.8% to 79.6%.<sup>9,21</sup> Therefore, while the southeastern United States has fairly high flea populations, there are areas in which *Bartonella* exposure may be less than expected.

In addition to serological testing for *T. gondii* and *Bartonella* spp. in this study, serological testing for viral causes of uveitis was also commonly completed. Seropositivity for FeLV was 2.68%, which was lower than previous studies investigating cats with uveitis (ranging from 0.9% to 12.1%).<sup>10,11,21–23</sup> Compared to a study investigating causes of feline uveitis in the same region 25 years prior, seropositivity is much reduced from the reported 11.3% of cases.<sup>22</sup> This is consistent with the overall reduction in the number of FeLV infected cats.<sup>45</sup> FeLV generally causes ocular disease due to the induction of lymphosarcoma and is not a major cause of primary ocular disease. This was demonstrated by one study which found that only 2% of cats infected with FeLV had clinical signs of ocular disease.<sup>3</sup> None of the cats in this present study that were diagnosed with FeLV had evidence of lymphoma, and likewise, none of the cats diagnosed with lymphoma were seropositive for FeLV, although one of the three cases diagnosed with lymphoma was not tested for the retrovirus. This makes interpreting the results of the FeLV seropositivity difficult, but it is likely that the positive results are incidental findings.

Like FeLV, the seropositivity for FIV in this study was found to be lower than previously reported values for cats with uveitis. In this study, 7.34% of cats tested were seropositive for FIV, and previous studies range from 3.8% to 22.9% in patients with uveitis.<sup>10,21–23</sup> However, unlike FeLV, ocular abnormalities, such as chronic ante-

rior uveitis and conjunctivitis, are much more commonly documented in cats with FIV.<sup>45</sup> One study, which experimentally infected twelve cats with FIV, found that all cats euthanized after three weeks (nine cats in total) had developed lymphoplasmacytic uveitis,<sup>46</sup> while another study found that thirteen of fifteen naturally infected cats had anterior uveitis at the time of euthanasia.<sup>6</sup> Therefore, it is likely that FIV infection contributed to the uveitis seen in the seropositive cats in this study.

Unlike FeLV and FIV, the seroprevalence of FCoV was slightly higher in this study than previous studies investigating feline uveitis, at 34.7% for all positive results, and 17.3% for titers >1:1600 or with positive PCR. To the authors' knowledge, the highest previously reported serological value in epidemiological studies of cats with uveitis was 27% for all seropositivity,<sup>23</sup> but when only cats with titers >1:1600 were included, the highest reported value was 5.6%.<sup>10</sup> As the titer rises, the likelihood of the titer being associated with FIP increases, as few healthy cats have titers of 1:1600, and titers greater than 1:3200 are highly suggestive of FIP.<sup>47,48</sup> In total, 19 cats (15.8%) in this study were ultimately diagnosed with FIP.

This percentage of FIP diagnoses is similar to the findings of Peiffer and Wilcock,<sup>4</sup> who performed a histopathological study of feline uveitis, that found 14.5% of eyes submitted for histopathology were diagnosed with suspected FIP based on the mixed neutrophilic, lymphoplasmacytic exudative inflammation present in those eyes. In addition, a full necropsy was performed on 7 (5.0%) additional cats that had lesions consistent with FIP and were diagnosed as confirmed FIP, for a total of 19.4% of feline uveitis cases being either suspected or confirmed FIP.<sup>4</sup> While that study had a biased toward severely damaged eyes requiring enucleation or cats with serious or fatal systemic diseases, our findings of 15.8% of cases being diagnosed with FIP is similar, and much higher than 2.2% of cases reported in the same region in 1991.<sup>22</sup> The average age of patients diagnosed with FIP in this study was 1.82 years, compared to the overall average of 7.62 years. Given the high percentage of cases diagnosed with FIP in this study, it is recommended that the minimal diagnostics for young cats presented with uveitis include FCoV serology and bloodwork to evaluate for hyperglobulinemia, which is reported in 50-70% of felines with FIP.<sup>49</sup>

In this study, only six cats (5.0%) were diagnosed with neoplasia, while previous epidemiological studies reported values of 13.2%<sup>22</sup> and 20.4%.<sup>4</sup> Only one case (0.8%) was a primary neoplasia, iris melanoma, which is the most common primary neoplasia of the eye, but not usually a cause of uveitis.<sup>2</sup> In this study, three cats (2.5%) were diagnosed with lymphoma, compared to 20.1% of cats in a previous study.<sup>4</sup> The previous study was a histopathological study, and thus, results were biased toward cases requiring enucleation or necropsy, while this present study was based on referrals to ophthalmologists.

Given that almost 50% of cats with newly diagnosed lymphoma have ocular abnormalities,<sup>50</sup> and a similar study from the same region performed in 1991<sup>22</sup> reported that 5.7% of cats presenting with uveitis were diagnosed with lymphoma, the number of cats diagnosed with lymphoma in this study was lower than expected. Considering that multiple types of neoplasia can present as focal growths and are possible to tentatively diagnose with a basic ophthalmic exam, it is possible that fewer patients with ocular neoplasia were referred.<sup>51</sup> Therefore, neoplasia, especially in older patients, as the average age of patients diagnosed with neoplasia in this study was 11.1 years, should still remain high on the differential list as a cause of uveitis.

While this study focused on neoplastic causes and five main infectious causes, it must be noted that there are multiple other causes of feline uveitis. *Cryptococcus neoformans*,<sup>12,13</sup> *Histoplasma capsulatum*,<sup>14</sup> *Blastomyces dermatitidis*<sup>15</sup> and *Coccidioides immitis*<sup>16,17</sup> have all been known to cause uveitis in feline patients. In this study, nine patients were tested for fungal disease, and one was diagnosed with cryptococcosis. The fact that only nine patients were screened for fungal disease is likely due to a combination of factors, one being that fungal agents tend to cause characteristic ocular lesions including granulomatous keratic precipitates, hypopyon, and granulomas within the retina and choroid, and often retinal detachment. In addition, most cats with uveitis from fungal agents are systemically ill, and therefore, a diagnosis is often made by identifying the fungal organisms at an extraocular site.<sup>2,18</sup> Therefore, despite the low number of tests, it is unlikely that this study underestimated the number of fungal uveitis cases. However, in areas where fungal disease is more common, including the southwestern United States or the Ohio, Missouri, and Mississippi river valleys, screening for fungal disease could be of further benefit in diagnosing the cause of endogenous uveitis.

Other possible causes of feline uveitis have been reported in the literature and should be considered as possible causes of uveitis. FHV-1 was first considered a possible cause of endogenous uveitis after a study found 14% of cats diagnosed with idiopathic uveitis had FHV-1 DNA in their aqueous humor, and significantly, more cats with idiopathic uveitis or with toxoplasmosis associated uveitis had FHV-1 antibodies in their aqueous humor than cats without uveitis.<sup>52</sup> However, a more recent study found that only 3.8% of cats with uveitis had positive PCR FHV-1 results in either their blood (1.9%) or aqueous humor (1.9%), while 31.6% of healthy cats had positive PCR results.<sup>21</sup> Thus, the association or causation of FHV-1 infection and uveitis is unclear and deserves more investigation. Additionally, case reports have documented other, rarely diagnosed, causes of uveitis, including aberrant larval migration of *Cuterebra* spp.,<sup>53,54</sup> leishmaniasis,<sup>55</sup> and mycobacteriosis.<sup>56</sup> Given that there are multiple causes of endogenous uveitis and the retrospective nature of this study, it is likely that some of the cases ruled idiopathic in this study actually had an infectious cause.

This study provides valuable information for the practicing veterinarian about the most commonly diagnosed causes of feline uveitis in North Carolina. In total, a definitive diagnosis was achieved in 30.8% of cases (37 cats), associated with neoplasia, FIP, FIV, FeLV, and cryptococcosis, and 40.8% of cases were ruled idiopathic. Finally, 29.2% (35 cases) of patients were seropositive for *Bartonella* spp, or *T. gondii*, or both and did not fit into either the definitively diagnosed cases or the truly idiopathic cases. This information should help guide client education on the benefits of pursuing initial diagnostics to find a definitive cause, which will likely be achieved one-third of the time. In addition, if toxoplasmosis or bartonellosis are not highly suspected, serology is a valuable test to rule out these diseases, as in this study only 23.7% of cats tested for *T. gondii*, and 43.2% of cats tested for *Bartonella* spp. were seropositive. This strategy would help avoid the expense and risks of unnecessary antibiotics and further diagnostic tests. If bartonellosis and toxoplasmosis are highly suspected, more definitive diagnostic tests, such as biopsies and histopathology for *T. gondii* and bacterial isolation for *Bartonella* spp., should be pursued. In addition, the most commonly diagnosed infectious disease was FIP (15.8% of cases). Therefore, especially in younger cats, FCoV serology and bloodwork should be performed to investigate FIP as the cause of uveitis. The occurrence of neoplasia in this study was lower than expected at 5.0%, but should remain as a differential, especially in older patients.

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