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Temporal occurrence and environmental risk factors associated with cytauxzoonosis in domestic cats

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Abstract

Cytauxzoon felis is a tick-transmitted protozoan parasite of domestic and wild felids in the south-central and southeastern United States. Infection of domestic cats (*Felis domesticus*) with *C. felis* is typically acute and characterized by fever, anorexia, listlessness, anemia, icterus and usually death within 19–21 days. To determine the temporal occurrence and environmental risk factors associated with infection of *C. felis* in domestic cats from Oklahoma, information in the electronic medical records from the Oklahoma Animal Disease Diagnostic Laboratory (OADDL) and Boren Veterinary Medical Teaching Hospital (BVMTH) was retrospectively searched. A total of 232 cytauxzoonosis cases from 1995 to 2006 from OADDL ($n = 180$) and 1998 to 2006 from BVMTH ($n = 52$) were combined and analyzed. The number of cytauxzoonosis cases remained relatively consistent from year to year. Diagnosis of *C. felis* infection in domestic cats followed a bimodal pattern with a peak in the number of cases in April, May, and June followed by a second smaller peak in August and September. The majority ($n = 72$; 31.0%) of cytauxzoonosis cases were diagnosed in May. No cases of *C. felis* infection were diagnosed in December and only a few ($n = 10$; 4.3%) cases were observed from November through March during the 12-year period. In cases for which the client's address was available, geographic coordinates were assigned and landscape characteristics were quantified within a 100-m radius of each cytauxzoonosis case location. Of cytauxzoonosis cases ($n = 41$) with a known client address, a majority ($n = 28$; 68.3%) occurred in low density residential areas and more cases ($n = 8$; 19.5%) were found in urban edge habitat than expected at random. Locations of diagnosed cytauxzoonosis cases were significantly associated with more wooded (31.8 ± 4.03%) cover and closer (55.5 ± 18.45 m) proximity to natural or unmanaged areas than randomly selected control sites. Practicing and diagnostic veterinarians can expect to see a distinct temporal pattern in cases of cytauxzoonosis and more cases can be expected in domestic cats living in close proximity to environments that support tick vectors and bobcats.

Keywords: *Cytauxzoon felis*; Cytauxzoonosis; Domestic cats; Environmental risk factors; Temporal occurrence; Oklahoma

1. Introduction

Cytauxzoon felis is a tick-borne protozoan parasite of domestic and wild felids. Originally reported in 1976 from domestic cats in southwestern Missouri (Wagner, 1976), *C. felis* is considered as an emerging infectious disease agent found throughout the south-central and

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southeastern United States (Birkenheuer et al., 2006; Hauck et al., 1982; Jackson and Fisher, 2006; Meinkoth and Kocan, 2005). Infection of domestic cats (*Felis domesticus*) with *C. felis* is acute and characterized by fever, anorexia, listlessness, anemia, icterus and usually death within 19–21 days (Wagner, 1976; Wagner et al., 1980). Historically, the mortality rate of cytauxzoonosis has approached 100%; however, clinical cases have been described in which cats survived infection both with and without treatment (Motzel and Wagner, 1990; Walker and Cowell, 1995). A focus of *C. felis*-survivor cats has been identified in a discrete geographic area ranging from western Arkansas to eastern Oklahoma (Meinkoth et al., 2000). Free-ranging and apparently healthy cats that survived infection of *C. felis* also have also been identified in Florida and Tennessee (Haber et al., 2007).

Cats become infected with *C. felis* sporozoites from tick bites. Within infected cats, *C. felis* first replicates asexually by schizogony in endothelium and macrophages lining organs (Kocan et al., 1992). Lungs, spleen, liver, and lymph nodes (Kier et al., 1987) are most noticeably infected although almost any organ is susceptible. The end products of schizogony are merozoites, which rupture the host macrophage and enter either a new host macrophage or erythrocyte. Within erythrocytes, the parasites, called piroplasms, have a characteristic signet-ring appearance and reproduce asexually through binary fission. The piroplasm can rupture erythrocytes; however, schizogonous replication of *C. felis* within macrophages is more pathogenic and results in the occlusion of vessels producing systemic disease (Kier et al., 1987).

Since infection of domestic cats is presumably dependent upon transmission of *C. felis* from ticks, the occurrence of disease seems to be limited to activity periods of tick vectors in enzootic areas. To date, the only experimentally confirmed vector of *C. felis* is *Dermacentor variabilis*, the American dog tick (Blouin et al., 1984). Infection of *C. felis* has been reported in three partially engorged *Amblyomma americanum*, lone star tick, nymphs recovered from a cat that died of cytauxzoonosis (Bondy et al., 2005). It is unclear whether the *A. americanum* ticks were infected prior to engorgement or if they ingested blood containing piroplasms from the vertebrate host while feeding. It also has been speculated (Hoover et al., 1994; Wightman et al., 1977) that cases of cytauxzoonosis are most often observed in rural cats free to roam in wooded areas. The purpose of the present study was to determine the temporal occurrence of cytauxzoonosis and to identify environmental risk factors associated with *C. felis* infection in domestic cats. Practicing and diagnostic veterinarians will benefit by knowing when to expect more cytauxzoonosis cases, what environmental factors are associated with infection, and how to effectively target parasite prevention efforts.

2. Materials and methods

2.1. Medical records

Electronic records from Boren Veterinary Medical Teaching Hospital (BVMTH) and Oklahoma Animal Disease Diagnostic Laboratory (OADDL), both in Stillwater, OK, were searched for cases of *C. felis* infection in domestic cats. Cases from 1998 to 2006 and 1995 to 2006 were reviewed from BVMTH and OADDL, respectively. Cytauxzoonosis cases were defined by either piroplasm detection on microscopic examination or by schizont detection through histopathology, with both detection methods predicated upon report of clinical signs characteristic of cytauxzoonosis. Data from BVMTH and OADDL were combined and analyzed according to the year and month of occurrence.

2.2. Geographical information system (GIS)

A street database based on 2000 TIGER/Line files from the Census Bureau for Oklahoma was obtained from geo information systems at the University of Oklahoma. Cases with client addresses were assigned geographic coordinates by linking street addresses for each case to the street database using ArcGIS® v.9.2 (Environmental Systems Research Institute, Redlands, CA). If a client address was unavailable or incomplete, then the record was excluded from the risk factor analysis. Once addresses were matched to geographical coordinates, each point was moved to the center of the home corresponding to the identified street location.

Landscape characteristics within a 100-m radius of each case location were quantified in order to represent the area of highest activity by domestic cats. Previous research suggested domestic cats typically remain close to their house of residence and move less than 100 m on a daily basis (Coleman and Temple, 1989; Kays and DeWan, 2004). Each case location was classified as occurring in low density residential or rural, high density residential, or urban edge areas using 2003 NAIP (National Agriculture Imagery Program) natural color positive images. Low density residential or rural areas included single family homes located on large (>50 m from another home) lots in urban or rural areas.

High density residential areas were represented by single family homes located within a defined housing community with homes <50 m apart. Urban edge areas were represented by homes adjacent to natural or low maintenance areas receiving limited management (e.g., mowing). The percent coverage of land use types was quantified within each buffer zone (i.e., circle with a 100-m radius) for agricultural, grassland, urban, water, and wooded habitats. The distance from each case location to the nearest natural or relatively unmanaged area was also estimated.

A majority of the cytauxzoonosis cases with known client addresses from BVMTH and OADDL were in the general vicinity of Stillwater, OK. Therefore, landscape characteristics associated with these cases were compared to those associated with random control sites within the same area to identify landscape factors associated with infection. Randomly generated points were used as controls because this method introduced less sampling bias than using uninfected cat locations. Randomly generated point locations were moved to the nearest home and the landscape characteristics described above were quantified for each control site.

2.3. Statistical analyses

The number of cytauxzoonosis cases according to year and month of occurrence were compared using the Kruskal–Wallis one-way analysis of variance on ranks (Sokal and Rohlf, 1997). A χ^2-test was used to compare the number of observed cytauxzoonosis cases versus the number of expected cytauxzoonosis cases that occurred at random in low density versus high density residential areas and cytauxzoonosis cases occurring within residential areas versus those at the urban edge. Mann–Whitney *U*-tests were used to compare land use cover types and distance to natural or unmanaged areas between observed cytauxzoonosis cases and randomly selected control locations (Sokal and Rohlf, 1997). Analyses were performed with SigmaStat 3.1 statistical software package (Systat Software, Point Richmond, CA).

3. Results

3.1. Temporal occurrence of cytauxzoonosis

A total of 232 cases from 1995 to 2006 and 1998 to 2006 from OADDL ($n = 180$) and BVMTH ($n = 52$) were analyzed, respectively. These cases of cytauxzoonosis represent approximately 1.0% and 1.5% of the total number of clinical cases of domestic cats at OADDL and BVMTH observed during the respective time periods. The number of cytauxzoonosis cases did not significantly differ ($H = 10.037$, d.f. = 11, $P = 0.527$; Fig. 1) from year to year. Diagnosis of *C. felis* infection in domestic cats followed a bimodal pattern with a peak in the number of cases in April, May, and June followed by a second smaller peak in August and September (Fig. 2). The majority ($H = 74.44$, d.f. = 11, $P < 0.001$) of cytauxzoonosis cases ($n = 72$) were diagnosed in May. No cases of *C. felis* infection were diagnosed in December and only a few ($n = 10$) cases were diagnosed from November through March during the 12-year period of analysis.

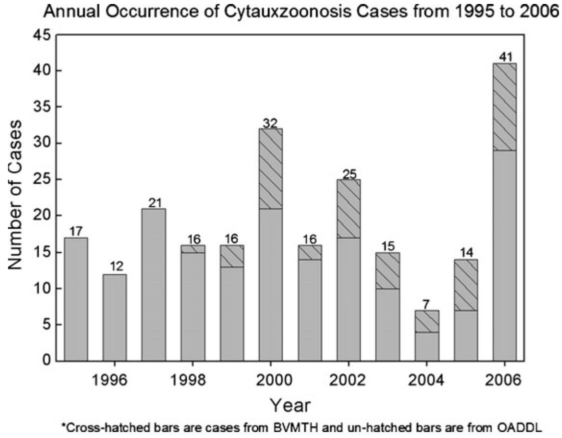

Fig. 1. Total number of cytauxzoonosis cases diagnosed at OADDL ($n = 180$ from 1995 to 2006) and BVMTH ($n = 52$ from 1998 to 2006).

3.2. Environmental risk factors associated with cytauxzoonosis

Geographic coordinates were obtained for 9 of the OADDL cases and 32 of the BVMTH cases (Fig. 3).

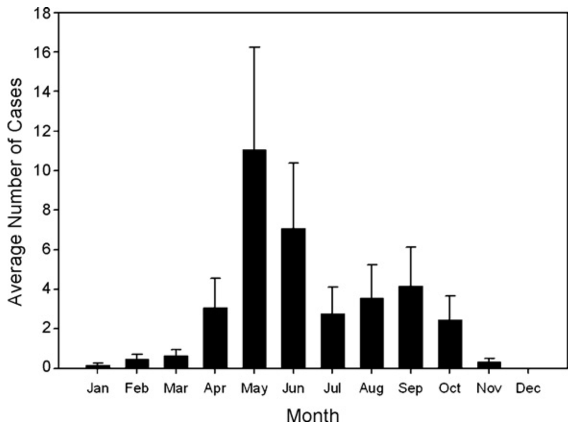

Fig. 2. Average (S.E.) number of cytauxzoonosis case per month. Data from OADDL and BVMTH combined.

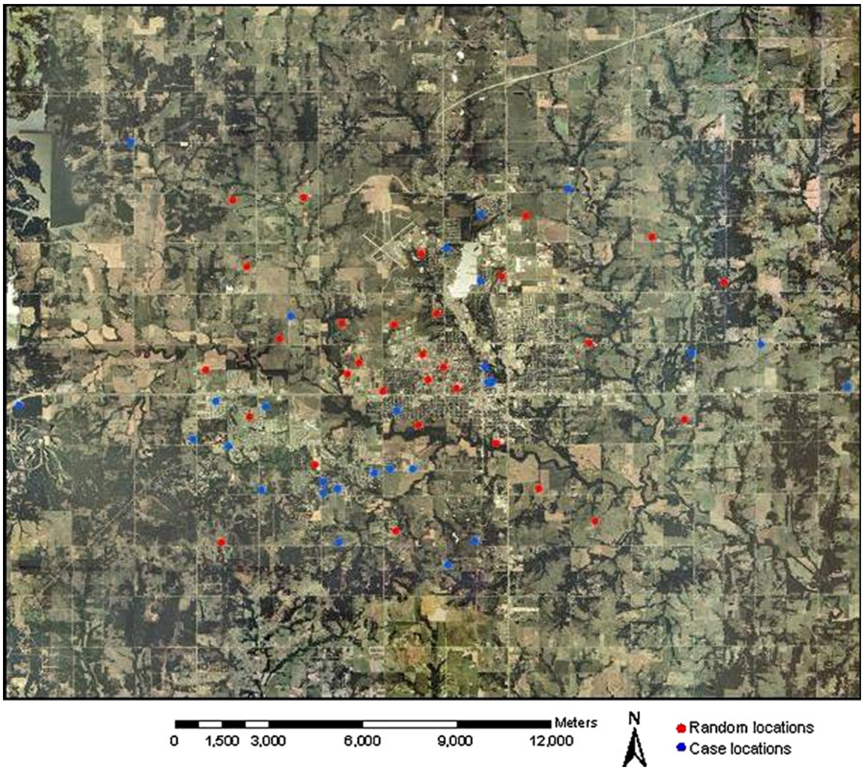

Fig. 3. Spatial locations of address matched cytauxzoonosis cases and random control sites in the Stillwater, OK area.

The majority ($n = 28$; 68.3%) of cytauxzoonosis cases occurred in low density residential or rural areas, with five (12.2%) cases in high density residential areas and eight (19.5%) cases in urban edge areas. Cases of cytauxzoonosis were associated with multiple land use cover types within 100 m of the residence (Fig. 4) and relatively short distances to the nearest natural or unmanaged area (Table 1). Even though 68.3% of the observed cases of cytauxzoonosis occurred in low density residential or rural areas, the locations of these cases did not differ significantly from those expected at random. However, significantly more ($\chi^2 = 13.393$, d.f. = 1, $P < 0.001$) cases ($n = 8$; 19.5%) cases occurred in urban edge habitat than expected at random. Case locations in the Stillwater area were significantly ($U = 637$, $P = 0.005$) associated with a higher percentage (31.8%) of wooded habitat and a closer proximity ($U = 706$, $P < 0.001$) to natural or unmanaged areas (55.6 $\pm$ 18.45 m) than randomly selected control locations (Table 1). Location of cytauxzoonosis cases did not differ for percent coverage of agriculture (4.9%; $U = 494$, $P = 0.330$), grassland (35.6%; $U = 489$, $P = 0.560$) or urban (27.2%; $U = 467$, $P = 0.80$) habitat. No cases of cytauxzoonosis were associated with water habitat.

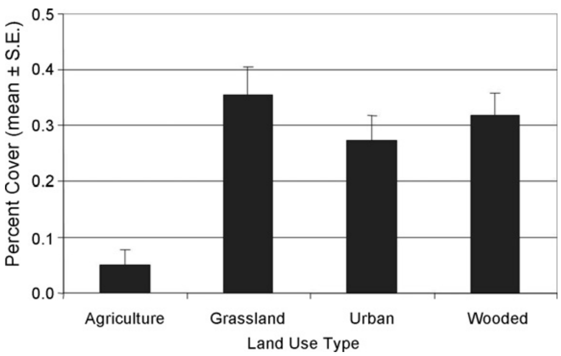

Fig. 4. Land use cover types within a 100-m buffer zone around address matched cytauxzoonosis cases.

4. Discussion

Infection of *C. felis* in domestic cats in enzootic areas results when the cats become incorporated into a naturally occurring cycle between bobcats (Blouin et al., 1984, 1987; Glenn et al., 1982), the normal vertebrate host, and tick vectors. Both bobcats (Rolley, 1985) and ticks (Wright and Barker, 2006) are abundant in Oklahoma. The number of cytauxzoonosis cases

Table 1
Land use cover types and distance to the nearest natural or unmanaged area for cytauxzoonosis cases and randomly selected control sites in the Stillwater, OK area

Landscape characteristic	Cases	Controls
Low density residential (*n*)	28	19
High density residential (*n*)	5	9
Urban edge (*n*)	8	2
% Agriculture (mean ± S.E.)	4.9 ± 2.92	11.3 ± 4.34
% Grassland (mean ± S.E.)	35.6 ± 4.81	40.2 ± 6.68
% Urban (mean ± S.E.)	27.2 ± 4.50	34.3 ± 5.89
% Wooded (mean ± S.E.)	31.8 ± 4.03	14.2 ± 3.24
% Water (mean ± S.E.)	0.00 ± 0.00	0.0 ± 0.00
Distance (m) to nearest natural or unmanaged area (mean ± S.E.)	55.5 ± 18.45	120.0 ± 18.08

diagnosed at OADDL and BVMTH remained consistent from year to year while the occurrence varied throughout the year. The largest number of cases were diagnosed in April, May and June (late spring/early summer), and were followed by another, smaller peak in August and September (late summer/early fall). Since bobcats remain active throughout the year and ticks have distinct seasonal variation in activity (Oliver, 1989), differences in the occurrence of cytauxzoonosis cases likely reflect variation in climatic conditions (Subak, 2003) and annual activity cycles of infected tick vectors. Seasonal activity of ticks can vary widely among geographical regions and can even differ within specific areas (Raghavan et al., 2007) depending on the availability of appropriate vertebrate hosts, suitable vegetation, and tick species (Oliver, 1989).

For the two ticks known or suspected to transmit *C. felis* to domestic cats, both *D. variabilis* and *A. americanum* are present in Oklahoma (Wright and Barker, 2006) and feed on domestic cats. In Oklahoma, *D. variabilis* is most active in spring and early summer where *A. americanum* is active from early spring to late fall (Wright and Barker, 2006). Both ticks can be found along wooded habitats (Wright and Barker, 2006) and in urban environments (Reichard, unpublished data). Further research will be necessary to elucidate the role of these two ticks for maintaining *C. felis* infection among felids and in transmitting the protozoan parasites to domestic cats.

To our knowledge, the present study is the first to quantify environmental risk factors associated with cases of cytauxzoonosis. A majority of cytauxzoonosis cases occurred in low density residential areas and were associated with the presence of multiple land use cover types within the 100 m buffer zone. Low density residential areas included homes on large lots in urban and rural areas with greater spacing between homes and greater coverage of agriculture, grassland and wooded habitats than expected for high density residential areas. The presence of multiple land use cover types within the buffer zones also suggests close proximity to edge habitat and the presence of multiple boundary types within the buffer zones.

More cases were found in urban edge habitat than expected at random. This association with edge habitat suggests that the locations of diagnosed cases were significantly associated with closer proximity to natural or unmanaged areas than randomly selected control sites. Thus, the likelihood of infection increased with the presence of edge and closer proximity to natural or unmanaged areas. In the present study, a large proportion of cases with known client addresses were located in the southwest region of Stillwater, OK (Fig. 3). For approximately the last 15 years, southwest Stillwater has seen active urban growth and incursion into previously natural or unmanaged areas indicating that urbanization may factor in the transmission of *C. felis* to domestic cats; however, this hypothesis has yet to be rigorously tested. Locations of diagnosed cases also were significantly associated with more wooded cover than control sites. Wooded habitat and habitat edges represent suitable habitat for bobcats and other wild mammals (George and Crooks, 2006; Lovallo and Anderson, 1996; Riley, 2006; Rolley and Warde, 1985; Tigas et al., 2002), as well as ticks (Sonenshine and Mather, 1994). Additionally, Haber et al. (2007) suggest that healthy free-roaming domestic cats chronically infected with *C. felis* may serve as reservoir hosts in addition to infected bobcats. The role of chronically infected domestic cats as a competent vertebrate reservoir host to naïve cats in urban areas is intriguing and should be further investigated.

Landscape structure has been shown to influence the epidemiology of infectious diseases in wild and domestic animals by promoting interactions among pathogens, vertebrate hosts, and arthropod vectors (Bradley and Altizer, 2007; Despommier et al., 2006). For example, significantly more bobcats in rural areas were positive for feline calicivirus antibodies than bobcats in urban zones, indicating greater contact with domestic cats in rural areas (Riley et al., 2004). Landscape structure also has been shown to be important in the epidemiology of tick-borne diseases. A study on the landscape ecology of lyme disease (*Borrelia burgdorferi*) in a northern suburb of New York City showed that the abundance of *Ixodes scapularis* was positively correlated with property size (Maupin et al., 1991).

Cases of cytauxzoonosis in domestic cats have been reported in Missouri (Wagner, 1976), Arkansas, Florida, Georgia, Louisiana, Mississippi, Oklahoma, Texas (Meinkoth and Kocan, 2005), Kentucky (Jackson and Fisher, 2006), North Carolina, South Carolina, and Virginia (Birkenheuer et al., 2006). The present study was conducted in an area in which *C. felis* is enzootic; however, our estimates on the occurrence of cytauxzoonosis are underestimated since it is likely that not all cases that actually occurred during the study period were reported to BVMTH or OADDL. Seasonal activity of ticks in other geographic areas will be considerably different than in Oklahoma; however, the environmental risk factors identified in the present study for cats living near wooded areas will likely be similar for other areas enzootic for *C. felis* since ticks vectors occupy similar ecological niches throughout their range.

Identification of a distinct temporal pattern of occurrence and environmental risk factors for cases of cytauxzoonosis should be used by veterinarians to guide their diagnosis, treatment options, tick prevention, and client education. Current protocols for treating cats infected with *C. felis* have met with little continued success (Greene et al., 1999; Meinkoth and Kocan, 2005). No vaccine for cytauxzoonosis exists, and prevention is solely based on limiting exposure to ticks (Meinkoth and Kocan, 2005). Veterinarians in areas enzootic for *C. felis* are encouraged to prescribe acaricides and to stress tick avoidance through indoor cat housing during times of peak disease occurrence. Finally, for veterinary clientele who find such preventive measures impractical, a strong case can be made for antibiotic chemoprophylaxis during times of peak disease occurrence. Although clinical trials would be required to validate this idea, select a practical drug, and titrate an effective preventive dose, early (i.e., subclinical) stages of *C. felis* in domestic cats theoretically should be susceptible to drugs currently used for treatment and thought to have some efficacy against cytauxzoonosis.

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