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Cat scratch disease: U.S. Clinicians' experience and knowledge

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Summary

Cat scratch disease (CSD) is a zoonotic infection caused primarily by the bacterium Bartonella henselae. An estimated 12,000 outpatients and 500 inpatients are diagnosed with CSD annually, yet little is known regarding clinician experience with and treatment of CSD in the United States. Questions assessing clinical burden, treatment and prevention of CSD were posed to 3,011 primary care providers (family practitioners, internists, paediatricians and nurse practitioners) during 2014-2015 as part of the annual nationwide DocStyles survey. Among the clinicians surveyed, 37.2% indicated that they had diagnosed at least one patient with CSD in the prior year. Clinicians in the Pacific and Southern regions were more likely to have diagnosed CSD, as were clinicians who saw paediatric patients, regardless of specialty. When presented with a question regarding treatment of uncomplicated CSD, only 12.5% of clinicians chose the recommended treatment option of analgesics and monitoring, while 71.4% selected antibiotics and 13.4% selected lymph node aspiration. In a scenario concerning CSD prevention in immunosuppressed patients, 80.6% of clinicians chose some form of precaution, but less than one-third chose the recommended option of counseling patients to treat their cats for fleas and avoid rough play with their cats. Results from this study indicate that a substantial proportion of U.S. clinicians have diagnosed CSD within the past year. Although published guidelines exist for treatment and prevention of CSD, these findings suggest that knowledge gaps remain. Therefore, targeted educational efforts about CSD may benefit primary care providers.

KEYWORDS

Bartonella henselae, cat scratch disease, *Ctenocephalides felis*, immunocompromise, lymphadenopathy, vector-borne disease

1 | INTRODUCTION

Cat scratch disease (CSD) is an infection typically caused by the bacterium *Bartonella henselae* and less commonly by newly recognized species such as *Bartonella clarridgeiae* (Angelakis & Raoult, 2014; Kordick, Hilyard et al., 1997). Cat fleas are responsible for spreading the bacterium among cats that in turn pass it to humans through scratches or bites. Estimated annual incidence of CSD in the United States ranges from 4.5 to 9.3 outpatient diagnoses per 100,000 population and 0.19–0.86 hospital admissions per 100,000 (Jackson, Perkins, & Wenger, 1993; Nelson, Saha, & Mead, 2016). Incidence of both outpatient and inpatient diagnoses is highest among children 5–9 years of age. Significant regional variation in CSD incidence is related to flea abundance, with the highest incidence occurring in the warm, humid climate of the South and the lowest incidence occurring in arid, mountainous regions.

Typical CSD is characterized by development of a papule at the site of inoculation that lasts days to weeks and proximal regional lymphadenopathy that lasts weeks to months (Angelakis & Raoult, 2014; Florin, Zaoutis, & Zaoutis, 2008). Patients may also experience fever, chills and malaise. Atypical CSD occurs in 5%-14% of cases in immunocompetent patients and may present with a wide range of

clinical manifestations, including Parinaud's oculoglandular syndrome, neuroretinitis, encephalitis, hepatosplenic lesions, osteomyelitis, endocarditis and fever of unknown origin (Bass, Vincent, & Person, 1997; Florin et al., 2008; Margileth, 2000). Immunocompromised patients are at particularly high risk of disseminated infection and may also develop bacillary angiomatosis or peliosis.

The epidemiology of B. henselae bacteraemia in cats has important implications for prevention, particularly for immunocompromised persons. One study of cats in northern California demonstrated that 39.5% were bacteraemic, with risk factors for bacteraemia including age <1 year. outdoor roaming, impounded/former stray status and flea infestation (Chomel, 1995). A case-control study in Connecticut found that cat-owning patients who contracted CSD were 15 times more likely to have a kitten (<1 year old) and 29 times more likely to have a kitten with fleas than cat-owning patients without CSD (Zangwill et al., 1993). Thus, prevention should focus on avoiding high-risk adoptions such as kittens or previous strays, limiting the spread of infection by treating cats for fleas and avoiding rough play with cats (Masur et al., 2014). Testing or treating cats for B. henselae is not recommended as seropositivity in cats does not necessarily indicate active bacteraemia, and treatment may carry significant risks such as increasing antibiotic resistance without any proven benefits (Brunt, Guptill, Kordick, Kudrak, & Lappin, 2006; Kordick, Papich, & Breitschwerdt, 1997; Masur et al., 2014).

CSD-associated lymphadenopathy is usually self-limited and believed to be the result of immune reactivity with granuloma formation rather than persistent infection (Lin et al., 2006). Antibiotic treatment for uncomplicated CSD may decrease lymph node size and time to resolution; however, no studies, to date, have shown a sustained improvement in outcome with antibiotic treatment (Angelakis & Raoult, 2014; Bass et al., 1998; Rolain et al., 2004). As a result, antibiotics are typically not recommended for immunocompetent individuals with uncomplicated CSD (Angelakis & Raoult, 2014). Lymph node aspiration is rarely indicated for CSD due to inherent risks such as infection and fistula formation, but may be used in cases of suppurative nodes for symptom relief or when the diagnosis is unclear.

Despite advances in knowledge of CSD epidemiology and burden of disease (Nelson et al., 2016), relatively little is known about clinician practices for diagnosis, treatment and prevention of CSD. Such information would provide important insight into regional trends, risk factors for CSD and practitioner knowledge of CSD. Additional data on knowledge gaps would also help tailor education and resources. The objectives of this study were to describe the national patterns of clinician-diagnosed CSD and assess clinician knowledge of clinical guidelines using data from a national survey of health care providers.

2 | MATERIALS AND METHODS

DocStyles is an annual, cross-sectional, nationwide survey of U.S. clinicians conducted by Porter Novelli Public Services, a public relations firm (Porter Novelli, 2006). Clinicians are randomly selected from the SERMO Global Medical Panel (www.sermo.com), which includes over 270,000 medical professionals in the United States. The total number

Impacts

- Among a nationally representative sample of primary care providers, 37.2% had diagnosed at least one patient with cat scratch disease in the past year.
- Primary care providers who see paediatric patients and practice in the Pacific and Southern regions were more likely to have diagnosed cat scratch disease.
- Although current guidelines recommend analgesic treatment and monitoring for patients with uncomplicated cat scratch disease, only 12.5% of providers chose this option for a hypothetical patient described in this survey, while 71.4% of providers would prescribe antibiotics, and 13.4% would aspirate the enlarged lymph node.

of respondents in the survey was pre-determined by Porter Novelli to align with the known demographics and specialties of practitioners in the United States. Quotas were filled on a first-come, first-served basis. Respondents were screened to include only those who practice in the United States; actively see patients; work in an individual, group, or hospital practice and have been practicing for at least 3 years.

The anonymized, web-based DocStyles 2014 and 2015 surveys contained 91 and 131 questions, respectively, covering a wide range of topics. Information on basic provider and practice characteristics was collected as part of the survey, and the Centers for Disease Control and Prevention licensed specific results from the survey related to CSD. Questions regarding CSD were limited to family practitioners, internists, paediatricians and nurse practitioners. Analysis of DocStyles 2014 and 2015 data was judged to be exempt from institutional review board requirements.

In total, three questions regarding CSD were asked of survey respondents. The 2014 survey included questions 1 and 2, while the 2015 survey included questions 2 and 3. The questions are outlined below with the preferred responses in bold where applicable:

Q1: In the past year, how many patients did you diagnose with cat scratch disease? Select one:

None 1-5 patients 6-10 patients 11-25 patients 26-100 patients >100 patients

(Note: For the purposes of analysis, responses were grouped into two categories: "None" and "≥1 patient")

Q2: A 16 year-old-female presents with axillary lymphadenopathy and low-grade fever. She adopted a kitten 4 weeks ago and has received multiple scratches on her arms while playing with it. Physical exam reveals a small papule on the right forearm and a 2×4 cm right axillary node with mild tenderness and overlying Recommend analgesics and monitor the patient Prescribe antibiotics and monitor the patient Recommend analgesics and aspirate the node Prescribe antibiotics and aspirate the node None of these

(Note: For the purposes of analysis, the responses involving aspiration were grouped into the single category "aspirate node")

Q3: Cats and their fleas are reservoirs for *Bartonella henselae*. An immunocompromised patient who owns a cat should be counseled to: (Select one)

Give the cat away **Avoid rough play with cat & treat for fleas** Test cat for Bartonella/Treat cat if positive Take no special precautions Don't know

All probabilities were generated using SAS JMP v. 10.0.0 or SAS 9.4 (SAS Institute, Cary, NC). Pearson chi-square analysis was performed for each category of responses. Unless otherwise stated, the reported chi-square result was generated based on the dichotomous comparison of the variable frequency against the combined frequency of all other possible results. In addition, backwards stepwise multivariate logistic regression using the generalized logit model was performed for each question to examine the interactions between multiple clinician characteristics and their answers. Variables included the answer categories defined above. The reference categories were "None" in the case of Question 1, "None of these" in the case of Question 2 and "Take no special precautions" for Question 3. Predictors used in the regression analysis were clinical practice setting, inclusion of paediatric patients, region and specialty, along with all possible two-predictor combinations. All predictors were parameterized using effects coding. Predictors were removed stepwise from the regression analysis if pvalues were ≥.05.

3 | RESULTS

Invitations were sent to 2,148 practitioners in 2014 and 1,934 practitioners in 2015, resulting in 1,510 (70.3%) and 1,501 (77.6%) respondents, respectively. Baseline characteristics of respondents are summarized in Table 1 and were similar between 2014 and 2015 (data not shown). The majority of clinicians worked in the outpatient setting (85.4%); nurse practitioners (24.4%) and internists (23.7%) worked in the inpatient setting more frequently than paediatricians (11.6%) and family practitioners (2.4%). Most clinicians (72.9%) reported seeing some paediatric patients (patients \leq 17 years of age), including 94.4% of family practitioners, 60.9% of nurse practitioners and 43.6% of internists.

TABLE 1 Demographic and practice characteristics of clinician

 respondents to the 2014 and 2015 DocStyles surveys

	Number (%)
Total respondents	3,011 (100)
Practitioner type	
Family practitioner	1,007 (33.4)
Internist	1,001 (33.2)
Paediatrician	502 (16.7)
Nurse practitioner	501 (16.6)
Practice setting	
Group outpatient	2,033 (67.5)
Individual outpatient	537 (17.8)
Inpatient	441 (14.6)
Years of practice	
<10 years	901 (29.9)
≥10 years	2,110 (70.1)
Sees paediatric patients ^a	
Yes	2,194 (72.9)
No	817 (27.1)
Patients per week	
<100	1,203 (40.0)
≥100	1,808 (60.0)
Region of practice ^b	
South	1,012 (33.6)
Northeast	745 (24.7)
Midwest	678 (22.5)
Pacific	403 (13.4)
Mountain	173 (5.7)
Gender	
Male	1,838 (61.0)
Female	1,173 (39.0)
Age	
≤40 years old	1,070 (35.5)
>40 years old	1,941 (64.5)

^aBased on response to the question "Do you ever see paediatric patients (children age 17 or younger)?"

^bRefer to Figure 1 for regions. Midwest includes IA, IL, IN, KS, MI, MN, MO, NE, ND, OH, SD and WI; Mountain includes AZ, CO, ID, MT, NM, NV, UT and WY; Northeast includes CT, MA, ME, NH, NJ, NY, PA, RI and VT; Pacific includes AK, CA, HI, OR, WA; South includes AL, AR, DE, District of Columbia, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA and WV.

In 2014, 37.2% of clinicians surveyed had diagnosed at least one case of CSD in the prior year (Table 2). When compared with all other clinicians, family practitioners (40.6%, p = .04) and paediatricians (47.2%, p < .001) were more likely to have diagnosed CSD, whereas nurse practitioners were less likely (21.2%, p < .001). Additionally, clinicians who saw some paediatric patients were significantly more likely to have seen at least one case of CSD (41.8%, p < .001). This trend remained significant even with removal of paediatricians and



 Incidence per 100,000
 39.9%

 % who have diagnosed ≥1 patient with CSD in past year
 South

FIGURE 1 Cat-scratch disease incidence, clinician experience, and treatment decisions by region. Incidence data adapted from Nelson et al., Cat Scratch Disease in the United States, 2005–2013, Emerg Infect Dis 2016. The region with the highest incidence (South) is highlighted in dark grey. For this map, AK and HI were not included in incidence calculations for the Pacific region

family practitioners from the analysis, with nurse practitioners and internists who saw paediatric patients being more likely to have diagnosed CSD in the prior year relative to their counterparts who did not see paediatric patients (38.1% versus 23.7%, respectively, p < .001).

Clinicians in the Pacific region were more likely to have diagnosed CSD compared to other regions of the country (44.2% versus 36.1%, p = .03) (Figure 1). The Mountain region had the lowest number of clinicians who had diagnosed CSD (27.6%, p = .06). Multivariate analysis was consistent with the chi-square analysis, identifying clinician specialty (p < .001), paediatric patient population (p < .001) and region of practice (p = .01) as strong predictive variables for diagnosing cases of CSD in the prior year.

In regard to management of a hypothetical 16-year-old patient with uncomplicated CSD (Q2), only 12.5% of clinicians chose the recommended treatment option of "analgesics and monitoring" (Table 2). Paediatricians (20.1%, p < .001) and physicians with paediatric patients (13.5%, p = .003) were more likely to choose the preferred option. Across all clinicians, "antibiotics and monitoring" was the most common choice, particularly among family practitioners (75.4%, p < .001). A total of 13.4% of respondents chose to aspirate the lymph node, with internists (17.1%, p < .001) and clinicians in the inpatient setting (17.2%, p = .01) being more likely to choose aspiration than their counterparts. When specialty is controlled for, however, inpatient nurse

practitioners were nearly twice as likely as their outpatient counterparts to select aspiration (20.5% versus 11.1%, p = .01), whereas there was no significant difference between inpatient and outpatient internists (18.1% versus 16.8%), paediatricians (6.9% versus 8.3%) or family practitioners (16.7% versus 12.2%). Clinicians in the Mountain region were less likely to choose "analgesics and monitoring" (6.9%, p = .02), whereas clinicians in the South were the most likely to choose this approach (13.9%, p = .08). Findings on multivariate analysis were consistent with the chi-square analysis, identifying clinician specialty (p < .001) and having paediatric patients (p = .04) as significant predictors of treatment decisions.

In a question assessing knowledge of CSD prevention in an immunocompromised patient (Q3), 30.3% of respondents chose the preferred answer of "avoid rough play with the cat and treat for fleas" (Table 3). Paediatricians were more likely than other clinicians to select this option (36.4% versus 29.1%, p = .02). The most common choice (31.2% of respondents) was "test cat for *Bartonella*/treat cat if positive." In all, 80.6% of respondents chose some form of precaution, whereas only 3.5% of respondents chose "no special precautions," and 15.9% of respondents did not know. Multivariate analysis was consistent with findings on chi-square analysis, identifying clinician specialty (p < .001) as a significant predictor of decision-making in regard to CSD prevention.

	Q1 ^a : In the past year, how many patients did you diagnose with cat scratch disease?	$Q2^b$: A 16 year-old-female presents with axillary lymphadenopathy and low-grade fever. She adopted a kitten 4 weeks ago and has received multiple scratches on her arms while playing with it. Physical exam reveals a small papule on the right forearm and a 2 × 4 cm right axillary node with mild tenderness and overlying erythema. You diagnose cat-scratch disease. What would you do next?			
	≥1 patient	Analgesics and monitor ^c	Antibiotics and monitor	Aspirate node	None of these
	% Within each category ^d	Row % ^d	Row %	Row %	Row %
Total – % (n)	37.2 (561)	12.5 (375)	71.4 (2151)	13.4 (403)	2.7 (82)
Practitioner specialty					
Family practitioner	40.6	10.4*	75.4	12.3	1.9*
Internist	36.3	11.0	69.3	17.1	2.6
Paediatrician	47.2	20.1	70.1	8.2*	1.6
Nurse practitioner	21.2*	11.8	69.1	13.4	5.8
Region					
Midwest	35.8	11.9	71.2	14.5	2.4
Mountain	27.6	6.9 [*]	77.5	13.9	1.7
Northeast	33.2	13.4	68.9	14.1	3.6
Pacific	44.2	10.2	71.2	15.9	2.7
South	39.9	13.9	72.5	11.1*	2.5
Paediatric population					
Yes	41.8	13.5	72.2	11.7*	2.6
No	23.8 [*]	9.5*	69.3	18.0	3.2
Practice setting					
Outpatient	37.6	12.6	71.9	12.7*	2.8
Inpatient	34.0	11.3	68.9	17.2	2.5

Bold text denotes correct response. Bold italic text: significantly more frequent than expected (p < .05) based on chi-square analysis.

^aIncludes 2014 data only (1,510 respondents total). For the purpose of analysis, responses were grouped into two categories: ">1 patient" and "None". ^bIncludes 2014 and 2015 data (3,011 respondents total).

^cPreferred response according to current guidelines (Rolain et al., 2004, Angelakis & Raoult, 2014).

^dExcept first row where indicated otherwise.

*Significantly less frequent than expected (p < .05) based on chi-square analysis.

4 | DISCUSSION

This study provides important insights into the clinical burden of CSD in the United States and clinician knowledge of CSD prevention and treatment. More than one-third of clinicians surveyed reported having diagnosed at least one case of CSD in the prior year, with notable differences in burden among provider types, patient populations and regions. It is important for clinicians to understand regional patterns of CSD in the United States in order to optimize prevention and early recognition of CSD in the clinical setting.

CSD diagnoses varied markedly by region and largely correlated with previous studies of the epidemiology of CSD (Nelson et al., 2016). The number of clinicians in the Pacific region who had diagnosed CSD in the previous year, however, was higher than expected given a low calculated incidence for this region from insurance claims data. The reasons for this discrepancy are unclear and should be explored further. A 2004 study of *B. henselae* in pet cats from four U.S. regions found that cats in California and Florida had similar rates of bacteraemia (28% and 33%, respectively) and seropositivity (62% and 67%, respectively), suggesting that the risk to humans in these states might be similar (Guptill et al., 2004).

The overall lack of concordance of survey answers with current CSD treatment guidelines was remarkable. Only 12.5% of respondents correctly chose to treat a hypothetical patient with uncomplicated CSD with analgesics and monitoring, while 71.4% chose to treat with antibiotics. One likely reason for this is lack of awareness of published treatment guidelines (Angelakis & Raoult, 2014). This is understandable, however, given the challenges of keeping up with guidelines for the myriad conditions that primary care providers manage. Interestingly, a 2015 DocStyles study found that only 64% of physicians chose the correct dual treatment option of ceftriaxone

TABLE 3 Frequency of recommendations by survey respondents for prevention of CSD in immunocompromised patients. Bold text denotes correct response

	Q3 ^a : Cats and their fleas are reservoirs for <i>Bartonella henselae</i> . An immunocompromised patient who owns a cat should be counseled to:						
	Avoid rough play and treat for fleas ^b Row %	Give the cat away Row %	Test cat for <i>Bartonella/</i> treat cat if positive Row %	No precautions Row %	Do not know Row %		
Total – n (%)	455 (30.3)	286 (19.1)	469 (31.2)	52 (3.5)	239 (15.9)		
Practitioner specialty							
Family practitioner	30.8	17.8	32.0	5.2	14.2		
Internist	28.2	22.4	30.5	3.2	15.7		
Paediatrician	36.4	20.0	22.4*	4.0	17.2		
Nurse practitioner	27.9	13.1*	40.2	0.4*	18.3		
Region							
Midwest	31.4	18.6	27.2	3.0	19.8		
Mountain	29.1	18.6	36.0	3.5	12.8		
Northeast	30.5	20.1	29.4	3.7	16.3		
Pacific	33.3	20.1	33.8	2.5	10.3*		
South	28.4	18.3	33.4	4.0	15.9		
Paediatric population							
Yes	31.2	18.5	30.7	3.7	15.9		
No	28.1	20.5	32.6	2.8	16.0		
Practice setting							
Outpatient	30.2	18.3	31.4	3.4	16.6		
Inpatient	30.7	23.0	30.3	3.7	12.3		

Bold italic text: significantly more frequent than expected (p < .05) based on chi-square analysis.

^aIncludes 2015 data only (1,501 respondents total).

^bPreferred response according to current guidelines (Masur et al., 2014).

^{*}Significantly less frequent than expected (p < .05) based on chi-square analysis.

plus azithromycin for gonorrhoea, a condition that is much more common than CSD (Bornstein et al., 2017). Furthermore, providers may be hesitant to try and convince patients with CSD-related lymphadenopathy that antibiotics are not necessary. Nevertheless, our findings demonstrate a need for enhanced education and resources for both clinicians and patients regarding CSD treatment in the United States.

Across all specialties, clinicians who included some paediatric patients in their practice were more likely to have diagnosed CSD in the prior year. This is consistent with the known higher incidence of CSD in children (Nelson et al., 2016). It is also possible, however, that CSD is differentially under-recognized in adults. For example, one study demonstrated that elderly patients (>60 years old) have a relatively high incidence of CSD, but are more likely to present without lymphadenopathy and with more severe manifestations, which may result in delayed or missed diagnoses (Ben-Ami et al., 2005). Additional research on atypical manifestations of CSD in both children and adults would be helpful.

Notably, clinician specialty appears to play an important role in treatment decisions, with family practitioners being more likely to prescribe antibiotics, internists being more likely to aspirate and paediatricians being more likely to choose analgesics. Such differences may be expected with the differences in clinician training and patient populations. The choice of antibiotics may also be driven primarily by patient/provider preference rather than differences in knowledge. Additionally, inpatient nurse practitioners were nearly twice as likely as outpatient nurse practitioners to choose aspiration, which may be due to bias from previously caring for patients with complicated CSD or a general bias towards procedural interventions while seeing higher-acuity patients. Nevertheless, these results indicate that clinician and patient education may serve to limit the overuse of antibiotics and invasive procedures for otherwise benign and self-limited cases of CSD.

Although relatively few clinicians (30.3%) chose the preferred response of "avoid rough play with cat and treat for fleas" when confronted with an immunocompromised patient with a cat, the majority of clinicians chose some form of precaution. The most popular option chosen was "test cat for *Bartonella* and treat cat if positive," which is not recommended due to the poor predictive value of testing, lack of evidence for treatment of otherwise healthy cats and difficulty administering medication to cats (Brunt et al., 2006; Masur et al., 2014). Additionally, giving the cat away is generally not recommended due to the potential benefits that pet ownership provides. These results highlight the fact that although most clinicians recognize the risks of CSD in immunocompromised patients, both clinicians and patients might benefit from education regarding prevention in this high-risk population.

This study was subject to several limitations. First, although respondent characteristics aligned with the expected demographics of practitioners in the United States, sampling bias may still exist and limit generalizability. Second, nurse practitioners were not stratified as specialists versus general practitioners, limiting the comparisons that can be made among nurse practitioners of different practice types. Third, CSD diagnoses were self-reported by survey respondents with no means to verify true infections. Finally, we were unable to differentiate whether incorrect responses for treatment and prevention questions were due to lack of knowledge of guidelines or other factors such as practitioner preference or questionnaire fatigue.

5 | CONCLUSIONS

This survey of primary care clinicians in the United States reveals higher rates of CSD diagnoses by clinicians who see paediatric patients and highlights regional differences in the incidence and clinical burden of CSD. A high proportion of inaccurate responses to questions regarding CSD treatment and prevention reveals potential knowledge gaps among the primary care community. Education and enhanced resources targeted to general practitioners in highincidence regions may improve implementation of these guidelines, decreasing unnecessary treatments and preventing transmission in high-risk patients.

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