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Human tularaemia associated with exposure to domestic dogs— United States, 2006-2016

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Abstract

Dogs have been implicated in the zoonotic transmission of numerous pathogens. Whereas cats are known to transmit *Francisella tularensis* to humans via bite and other routes, the role of dogs in facilitating infection is much less understood. We reviewed tularaemia case investigation records collected through national surveillance during 2006–2016 to summarize those with dog involvement, characterize the nature of dog-related exposure and describe associated clinical characteristics. Among 1,814 human tularaemia cases, 735 (41%) supplemental case investigation records were available for review; and of those, 24 (3.3%) were classified as dog-related. Median age of patients was 51 years (range: 1–82); 54% were female. Two thirds (67%) of cases presented with ulceroglandular/glandular tularaemia; pneumonic (13%) and oropharyngeal (13%) illness occurred less frequently. Dog-related exposures were classified as follows: direct contact via bite, scratch or face snuggling/licking (n = 12; 50%); direct contact with dead animals retrieved by domestic dogs (n = 8; 33%); and contact with infected ticks acquired from domestic dogs (n = 4; 17%). Prevention of dog-related tularaemia necessitates enhanced tularaemia awareness and tick avoidance among pet owners, veterinarians, health care providers and the general public.

Keywords

dog; epidemiology; Francisella tularensis; One Health; tularaemia; zoonoses

1 | INTRODUCTION

Tularaemia is an uncommon but potentially serious zoonosis caused by the gram-negative coccobacillus, *Francisella tularensis* (Penn, 2015). Primarily a disease of the northern hemisphere, tularaemia has been reported from all U.S. states except Hawaii. *F. tularensis* circulates in nature among small mammals and is known to cause epizootics in reservoir hosts such as lagomorphs and rodents. Humans can be exposed to this highly infectious environmental bacterium in many ways. Typical exposure to *F. tularensis* occurs via the bite of an infected tick or deerfly, handling of infected animal carcasses, and less frequently by

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inhalation of contaminated aerosols or ingestion of contaminated food or water. Infection in humans manifests as several clinical forms, depending on the route of exposure, and can range from mild, localized illness to life-threatening infection. A total of 1,208 human cases were reported in the United States during 2001–2010; median patient age was 39 years and 68% were male (Centers for Disease Control & Prevention, 2013).

Francisella tularensis can also infect domestic pets, resulting in clinical illness in cats and less commonly in dogs (Feldman, 2003). The few examples of documented natural infection in dogs describe mild and self-limiting illnesses characterized by fever, lethargy and anorexia (Gustafson & DeBowes, 1996; Meinkoth, Morton, & Meinkoth, 2004). Human infection by direct contact with infected cats via bites or scratches has been well documented; however, the potential role of domestic dogs in facilitating human tularaemia is less clear (Capellan & Fong, 1993). Dogs have been implicated in transmission of *F. tularensis* to humans in more diverse ways than secondary transmission well documented for cats—for example, after mouthing infected animal carcasses, bringing infected ticks into the home, or aerosolizing contaminated particles by shaking or during shearing (Hughes, 1965; Martone, Marshall, Kaufmann, Hobbs, & Levy, 1979; Rumble, 1972; Siret et al., 2006; Teutsch et al., 1979).

Little is known regarding the scope and patterns of human tularaemia cases with exposures linked to domestic dogs. Here we summarize a series of human tularaemia cases with dog-related exposures to improve understanding of canine roles in transmission of *F. tularensis* to humans and to facilitate health care provider and public awareness.

2 | MATERIALS AND METHODS

In the United States, tularaemia is a nationally notifiable human illness. Cases are investigated by state and local health departments, and basic non-disease-specific information is reported voluntarily to the Centers for Disease Control and Prevention (CDC), including age, sex, and state and county of residence. Additional clinical information and exposure history are shared with CDC on tularaemia case investigation forms at the discretion of the reporting state. Collection of these supplemental data began in 2006 and is typically available for less than half of total reported cases. For surveillance, a confirmed case of tularaemia is defined as either isolation of *F. tularensis* in a clinical specimen or a 4-fold or greater change in serum antibody titre to *F. tularensis* or detection of antigen by fluorescent antibody assay on clinical specimens. Both probable and confirmed cases should be supported by compatible signs and symptoms (Centers for Disease Control & Prevention, 1999).

For this summary, we reviewed available confirmed and probable human tularaemia case investigation records from 2006–2016 and extracted those with potential evidence of domestic dog involvement—specifically, affirmative answers to standardized questions indicating contact with a pet dog that was ill, died, or brought home dead animals in the 2 weeks preceding human illness, or written comments that provided other evidence of dog-related exposure to *F. tularensis*. Two independent reviewers further evaluated the records in

detail to select those demonstrating dog-related *F. tularensis* exposure based upon strength of available evidence. Cases were excluded from being classified as dog-related if an exposure route unrelated to dog contact was identified as the likely source of infection (e.g., pneumonic tularaemia after mowing) or if the anatomic site of inoculation via dog bite/ scratch or dog-facilitated tick bite differed from that of local signs (i.e., lymphadenopathy or skin lesions). Cases with discordant reviewer classifications were re-examined by two additional independent reviewers to provide final determination on classification as dog-related tularaemia cases. We then conducted a detailed review of each case record to summarize information on patient characteristics, clinical illness and type of exposure. Dog-related exposures were classified into three groups: (a) direct contact via bites, scratches or face snuggling/licking; (b) contact with dead animals retrieved by domestic dogs; and (c) contact with ticks introduced by domestic dogs.

3| RESULTS

During 2006–2016, a total of 1,814 human tularaemia cases were reported nationally; 735 (41%) had available supplemental case investigation records. Among these 735 records, 220 (30%) contained any mention of a dog, indicated as a pet in response to standardized questions regarding domestic animal exposures and pet illness, or in the written comments section. Twenty-four (3.3%) of the 735 records were ultimately classified as cases of dog-related tularaemia and are summarized in Table 1. Median age of patients with dog-related tularaemia was 51 years (range: 1–82 years); 54% were female. Cases were most commonly reported from Missouri (n = 9; 38%), followed by Colorado (n = 3; 13%) and Kansas (n = 3; 13%); 1–2 cases each were also reported from Alaska, Arizona, Nebraska, New Mexico, Oregon and South Dakota. Month of illness onset ranged from April through September, with most cases occurring in July (n = 10; 42%), May (n = 5; 21%) and June (n = 5; 21%). Sixteen (67%) cases were ulceroglandular/glandular in presentation; others were classified as pneumonic (n = 3; 13%) and oropharyngeal (n = 3; 13%) tularaemia. Among 20 patients with known clinical outcomes, 18 (90%) recovered from illness and two (10%) died.

Twelve (50%) of the 24 case patients reported direct contact with a dog in the 14 days preceding illness onset. Percutaneous inoculations conceivably occurred through a dog bite or scratch in eight cases, of which six were ulceroglandular/glandular, one typhoidal and one oropharyngeal in presentation—the last associated with a bite wound on the neck. Close contact via face snuggling and licking after a dog's exposure to *F. tularensis* was suggested in the remaining four cases, three in which the dog was reportedly ill. Among these four patients with close facial contact with a dog, three patients had pneumonic tularaemia, typically the most severe clinical form, and the fourth was reported as glandular.

Eight (33%) of the 24 cases had contact with presumed infected rabbit or rodent carcasses brought home or retrieved by domestic dogs; in five cases, dead animals retrieved by dogs were found in the home environment and disposed of by the patient, while in three cases a carcass was specifically removed from a dog's mouth. Three patients were presumed to be inoculated through a pre-existing wound, a splinter or a cut, after handling a carcass—two while removing a dead rabbit from their dog's mouth and one while disposing of a carcass from the home environment. One dog that retrieved a carcass was noted to be ill, but was not

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evaluated for infection. Among the eight cases with rabbit/rodent exposure facilitated by dog hunting/retrieving behaviours, six were ulceroglandular/glandular and two were oropharyngeal in presentation. In one case, a one-year-old girl died after her oropharyngeal tularaemia progressed to pneumonia and meningitis. This patient had contact with rabbit and rodent carcasses brought into the house by family dogs.

Dogs were implicated in bringing ticks in contact with human hosts in four cases (17%), either carried on the fur (n = 3; 13%), or in one instance (4%) inoculating the owner's eye when the tick burst following removal from a dog. As expected by exposure route, the three patients with reported tick bites presented with ulceroglandular tularaemia, while the patient with ocular exposure to tick blood developed oculoglandular tularaemia.

Among the 24 dog-related human tularaemia cases, only four (17%) case records indicated exposure to ill dogs. Three of these patients had direct contact with ill dogs, while the remaining case record indicated both contact with an ill dog and that the pet had brought a dead animal home. Only one ill dog was evaluated for laboratory evidence of exposure to *E* tularensis—a single serum sample had a positive *E* tularensis-specific titre of 1:256. One additional dog not reported as ill was also evaluated by serologic testing, but results were negative.

4 | DISCUSSION

Dogs have been implicated in the transmission of F tularensis to humans infrequently in the literature. In this case series, we summarize 24 cases of human tularaemia in which domestic dogs were considered to play a role in facilitating human infection. These cases were associated with various types of exposures to domestic dogs, but all fell into three general categories; approximately half occurred via some type of direct contact with dogs, one third due to handling of carcasses retrieved by dogs, and the remainder due to tick-mediated transmission that was facilitated by domestic dogs. The diverse ways in which dogs can facilitate human exposure to F tularensis present several opportunities for prevention.

Dogs generally experience milder clinical illness and are less often reported as associated with human infection than their feline counterparts. Nevertheless, the potential for true secondary transmission from ill dogs exists. Despite limited detail on clinical illness of pet dogs in this specific case series, several cases associated with close contact with reportedly ill dogs add to available evidence that dogs not only facilitate human exposure to the bacterium, but are capable of secondary transmission to humans. One published case report, also included in our case series, involved close facial contact and co-sleeping with a dog that experienced a brief illness after catching a rabbit (Yaglom et al., 2017). In an additional published report, a woman developed tularaemia endocarditis after close contact with her free-roaming dog that had died unexpectedly after a brief illness (Salit, Liles, & Smith, 2013). Several cases included in this series had strong evidence of direct inoculation via dog bite, as described by wound infection and/or proximal lymphadenopathy; however, it can be challenging to discriminate true secondary transmission from passive mechanical transmission through a dog bite given generally mild clinical illness in dogs.

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Most dog-related human tularaemia involves increased opportunity for human exposure to the bacterium, including handling of infected animals and tick bites. Human tularaemia facilitated by the hunting and retrieving behaviours of dogs has been previously documented (Ey & Daniels, 1941; Martone et al., 1979; Nordstoga et al., 2014; Ryan-Poirier, Whitehead, & Leggiadro, 1990). Additionally, it is conceivable that persons could be exposed through mechanical transfer or aerosol distribution of F. tularensis on dogs' skin/coat or mouth, given the extremely low infective dose for humans—10 to 50 organisms when injected or inhaled under experimental conditions (Penn, 2015). Increasing evidence suggests that domestic pet ownership may facilitate human exposure to arthropod vectors of other zoonotic conditions, including plague and Lyme disease (Gould, Pape, Ettestad, Griffith, & Mead, 2008; Jones et al., 2017). Interestingly, the seemingly rare circumstance of oculoglandular tularaemia caused by inadvertently expressing blood from a tick removed from a pet dog, inoculating the eye of the owner, has been previously described in the literature (Hughes, 1965). Together these findings highlight opportunities to minimize human exposure facilitated by dogs, including care in handling of animal carcasses retrieved by dogs, careful tick removal and regular use of species-appropriate tick prevention methods to prevent illness not only for pets but also among pet owners.

The mild nature of tularaemia in dogs and difficulty in confirming infection may explain the lack of investigation into domestic canine sources of infection (Meinkoth et al., 2004). Among the four human case records summarized in this series in which the dog involved was reported to be ill, only one dog was evaluated for infection and had an elevated *F. tularensis-specific* titre. Several studies indicate that seroprevalence in domestic dogs from tularaemia-endemic areas is high, so a 4-fold change in titres is necessary to confirm recent infection (Markowitz et al., 1985; Schmid et al., 1983). However, even a single elevated titre to *F. tularensis* in a dog is informative in a tularaemia case investigation (Yaglom et al., 2017). Therefore, although not definitive evidence, serologic evaluation should be considered, especially if the dog was ill or had known risk factors such as hunting, retrieving rodent or lagomorph carcasses, or roaming.

The patients in this series were of higher median age (51 vs. 39 years) and more frequently female (54% vs. 32%) compared to all human tularaemia cases captured through national surveillance during 2001–2010 (Centers for Disease Control & Prevention, 2013). Median age did not differ between dog-related cases (51 years) and all tularaemia cases reviewed (52 years). However, the female pre-ponderance of dog-related cases remains when compared to all supplemental case records (54% vs. 34%). This may be attributed to the types of interactions females have with dogs, or that females are more likely to own dogs (Saunders, Parast, Babey, & Miles, 2017). However, data collection methods and the small size of this case series limit the interpretation of these differences.

There were several additional factors limiting the generalizability of findings from this case series. While tularaemia is a nationally notifiable condition, mild infections may go undiagnosed and consequently unreported to the public health system. Furthermore, selection of dog-related human tularaemia cases relied on the strength of available evidence, and some case records were excluded due to lack of sufficient detail to support dog-related exposure.

Although uncommon, the dog-related tularaemia infections summarized here highlight specific modifiable risk factors for pet owners to minimize their chances of exposure to *F. tularensis.* Veterinarians play a key role in ensuring that pet owners are aware of risks and opportunities for zoonotic disease prevention, including use of appropriate tick control products on dogs, careful removal of engorged ticks, wearing gloves to dispose of animal carcasses retrieved by dogs, avoiding direct facial contact with pets who hunt or roam and seeking veterinary care for ill pets. When tularaemia is identified in a dog or cat, public health officials should be notified for prompt investigation and to assess whether preventive measures in pet owners and veterinary staff as recommended by CDC should be implemented (Feldman, 2003). Using a One Health approach to tularaemia case investigations, public health officials should continue to assess potential animal exposures and consider involving veterinarians when suspicion of a domestic pet exposure source is high.

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Impacts

- Humans may be exposed to *Francisella tularensis* through direct contact with dogs or infected ticks or wild animal carcasses that dogs bring into contact with humans.
- Recognizing human and dog activities that are associated with transmission of *F. tularensis* is essential to preventing dog-related human tularaemia and other zoonoses with similar transmission routes.
- Pet owners should take precautions when disposing of animal carcasses retrieved by pet dogs, be encouraged to use veterinarian-recommended tick control products on their dogs, and exercise caution in direct facial contact with pets.

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Summary o

Case	State	Illness onset (month/year)	Age (y)	Sex	Type of exposure	Clinical presentation	Outcome
1	MN	5/2006	40	М	Hunting/retrieving	Ulceroglandular	Unknown
5	AK	6/2009	59	ц	Hunting/retrieving	Ulceroglandular	Recovered
3	SD	5/2010	1	Ц	Hunting/retrieving	Oropharyngeal	Died
4	OM	7/2011	4	Ц	Ticks	Oculoglandular	Recovered
5	OM	6/2012	62	М	Ticks	Ulceroglandular	Recovered
9	KS	7/2012	42	Ц	Hunting/retrieving or direct contact	Ulceroglandular	Recovered
7	OM	9/2012	49	Ц	Ticks	Ulceroglandular	Recovered
8	OM	4/2013	51	М	Direct contact	Typhoidal	Unknown
6	KS	5/2013	51	М	Direct contact	Pneumonic	Recovered
10	NE	5/2013	24	М	Ticks	Ulceroglandular	Recovered
11	SD	5/2014	50	М	Direct contact	Pneumonic	Unknown
12	CO	8/2014	51	Ц	Hunting/retrieving	Ulceroglandular	Recovered
13	CO	6/2015	27	ц	Direct contact	Glandular	Recovered
14	MN	7/2015	51	М	Hunting/retrieving	Glandular	Recovered
15	OR	7/2015	66	М	Hunting/retrieving	Ulceroglandular	Recovered
16	OR	7/2015	60	ц	Hunting/retrieving	Oropharyngeal	Recovered
17	OM	7/2015	49	М	Direct contact	Ulceroglandular	Recovered
18	OM	4/2016	82	М	Direct contact	Ulceroglandular	Recovered
19	AZ	6/2016	73	ц	Direct contact	Pneumonic	Died
20	ОМ	6/2016	10	ц	Direct contact	Oropharyngeal	Recovered
21	KS	7/2016	4	ц	Direct contact	Glandular	Recovered
22	ОМ	7/2016	51	ц	Direct contact	Ulceroglandular	Recovered
23	ОМ	7/2016	61	М	Direct contact	Ulceroglandular	Unknown
24	CO	7/2016	LL	Ц	Direct contact	Ulceroglandular	Recovered