The Conflicting Roles of Vector Control and Animal Control Agencies in Mitigating the Rise of Human Cases of Flea-borne Typhus in Orange County, California

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ABSTRACT: Flea-borne typhus has emerged as an important vector-borne disease in Los Angeles and Orange Counties, California, with over 400 human cases having been reported since the mid-1980s. In Orange County alone, 127 human cases have been investigated by the Orange County Vector Control District since 2006. Results from a collaborative study with the Centers for Disease Control and Prevention from 2006-2008 identified the suburban cycle of flea-borne typhus transmission (backyard wildlife/pets – fleas – humans) in Los Angeles and Orange counties. Free-ranging feral and companion cats and the Virginia opossum were identified as the primary host animals of the cat flea, the insect vector responsible for maintenance and transmission of the etiologic agents, *Rickettsia typhi* and *R. felis*, for disease in humans. Although the causes of the increase in human flea-borne typhus cases are not well-defined, this rise has been accompanied by changes in how public and privately-sponsored animal control groups manage nuisance animal populations in the affected southern California counties. Instead of elimination through euthanasia of unwanted feral cats and non-native opossums, rehabilitation, relocation, and "no-trap" policies have become the preferred practice of local animal control agencies. The public health obligation for which governmental animal control agencies were created must be re-emphasized as one way of preventing further outbreaks of flea-borne typhus infections in Orange County and the surrounding California counties.

KEY WORDS: cat flea, *Ctenocephalides felis*, *Didelphis virginiana*, disease, *Felis catus*, feral cats, flea-borne typhus, public health, *Rickettsia felis*, *Rickettsia typhi*, trap-neuter-return, vector-borne disease, Virginia opossum

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INTRODUCTION

Flea-borne typhus (i.e., flea-borne rickettsiosis) is a zoonotic disease caused by either of two gram-negative, obligate intracellular bacteria: *Rickettsia typhi* and *R. felis*. Both rickettsial pathogens are found worldwide and are dependent on specific arthropod vectors and mammalian hosts to maintain their life cycles. Flea-borne typhus is considered to be one of the most widespread arthropod-borne diseases in the world, with most human cases occurring in tropical and subtropical regions, often near seaports (Azad et al. 1997). Humans and other mammals (neither rickettsial species is known to affect host animals) typically acquire the infection through a flea bite, inhalation, or contact with rickettsia-containing flea feces or crushed flea tissue rubbed into the bite wound, eyes, nose, or mouth (Azad 1990). In humans, symptoms for either pathogen are similar, appear 6-14 days after infection, and may include fever, rash, and headache, sensitivity to light, myalgia, and neurologic complications (Civen and Ngo 2008). Illness ranges from mild to severe, depending on the age and health of the victim; based on serological surveys, most infections are self-limited and are never diagnosed (Azad et al. 1997). However, among medically-recognized cases, patients with flea-borne typhus often require hospitalization if not treated promptly with antibiotics (e.g., doxycycline); the case-fatality rate is only about 2% in the U.S. (Azad and Beard 1998).

R. typhi is the causative agent of the first recognized form of flea-borne typhus, murine typhus (Dyer 1944), and is classically maintained in a rat-flea-rat transmission cycle among urban rats, *Rattus norvegicus* and *R. rattus*, and the Oriental rat flea, *Xenopsylla cheopis*, although other animals and flea species can be involved (Traub et al. 1978, Azad 1990). Historically in the U.S., *R. typhi* epidemics were associated with heavy rat and flea infestations and occurred frequently in California, Texas, and the southeastern states, resulting in thousands of human cases annually through the mid-1940s (Azad 1990). A combination of environmental modifications and rat/flea control public health campaigns led to a dramatic decline to <100 diagnosed *R. typhi* infections annually in the U.S. by 1980 (Azad et al. 1997).

Rickettsia felis was discovered in 1990 (Adams et al. 1990) and unlike *R. typhi* is maintained primarily in a zoonotic transmission cycle involving the cat flea, *Ctenocephalides felis*, and domestic and peridomestic animals (Williams et al. 1992, Azad et al. 1997). *Rickettsia felis* was identified as a human pathogen in 1994 (Schriefer et al. 1994), and the term "cat flea typhus" has sometimes been used to specifically describe infection with this bacterium. However, most patients infected with *R. felis* are diagnosed as having murine typhus because of similarity of symptoms and serologic cross-reactivity to the *R. typhi* antigen used in standard diagnostic tests (Schriefer et al. 1994, Civen and Ngo 2008, Pérez-Osorio et al. 2008). Because of its association with the ubiquitous cat flea, *R. felis* is now recognized as an emergent threat to human health (Pérez-Osorio et al. 2008). Co-infections with *R. typhi* have been found in cat and rat fleas (Noden et al. 1998, Eremeeva et al. 2008, Karpathy et al. 2009, Abramowicz

et al. 2011, Eremeeva et al. 2012, Nogueras et al. 2013) and in vertebrate hosts (Boostrom et al. 2002, Abramowicz et al. 2011), but are relatively infrequent. Co-infections of *R. typhi* and *R. felis* are possible in humans but would be diagnostically indistinguishable unless a serologic assay with *R. felis* antigen or molecular tests, such as a quantitative PCR (qPCR) (Henry et al. 2007), are used.

In the U.S., human cases of flea-borne typhus have been increasing since the 1990s and now average about 200 annually, occurring primarily in south-central Texas, Hawaii, and southern California (CDPH 2014). Recent studies using molecular methods (qPCR) have shown that *R. felis* is overwhelmingly the most abundant rickettsial pathogen found in infected fleas in endemic areas (Boostrom et al. 2002, Eremeeva et al. 2008, Abramowicz et al. 2011, Eremeeva et al. 2012). As has been noted with the increase in human flea-borne typhus cases in southern California and Texas, the ecological characteristics of the disease transmission cycle have changed from the classical urban, commensal rodent - rat flea cycle to a complex suburban cycle involving opossums (*Didelphis virginiana*), cats (*Felis catus*), and cat fleas (Adams et al. 1970, Schriefer et al. 1994, Boostrom et al. 2002, Reif and Macaluso 2009).

Opossums, cats, dogs (*Canis familiaris*), and other similarly-sized mammals [raccoons (*Procyon lotor*) and stripped skunks (*Mephitis mephitis*)] are widely abundant around homes in suburban southern California and Texas. Ecologic investigations of flea-borne typhus outbreaks in these areas have shown that the cat flea is the primary flea species parasitizing backyard wildlife and companion animals (Azad et al. 1997, Reif and Macaluso 2009). Cat fleas feed frequently and indiscriminately, change hosts often, and will readily bite humans (Rust and Dryden 1997), availing them with many opportunities to acquire and transmit pathogens among their hosts. In Orange and Los Angeles Counties, approximately 48% of cat fleas tested positive for *R. felis*, whereas less than 2% were found infected with *R. typhi* (Eremeeva et al. 2012). Together, both ecologic and epidemiologic studies suggest that backyard wildlife, such as opossums and free-roaming cats, maintain populations of cat fleas in the environment that infest companion cats and dogs not currently on flea control. Companion cats and dogs bring *R. felis*-infected fleas into the home environment where they may transmit the pathogenic rickettsial bacteria to their owners (Reif and Macaluso 2009, Eremeeva et al. 2012).

Until 2000, Los Angeles County averaged 3-21 flea-borne typhus cases annually but has experienced a dramatic rise since 2006, both in numbers and spatial distribution of flea-borne typhus cases in areas where the disease was not usually found (Civen and Ngo 2008). In Orange County, California, prior to 2006, human cases of flea-borne typhus averaged <20 cases/decade (Figure 1). Recently, 127 suspected, probable, and confirmed human cases have been reported in the last 7 years, paralleling the increase in neighboring Los Angeles County (Figure 2). This paper will discuss some of the factors that may be contributing to the increase in human flea-borne typhus cases in Orange County and the Orange County Vector Control District's efforts to mitigate disease prevalence in the county.

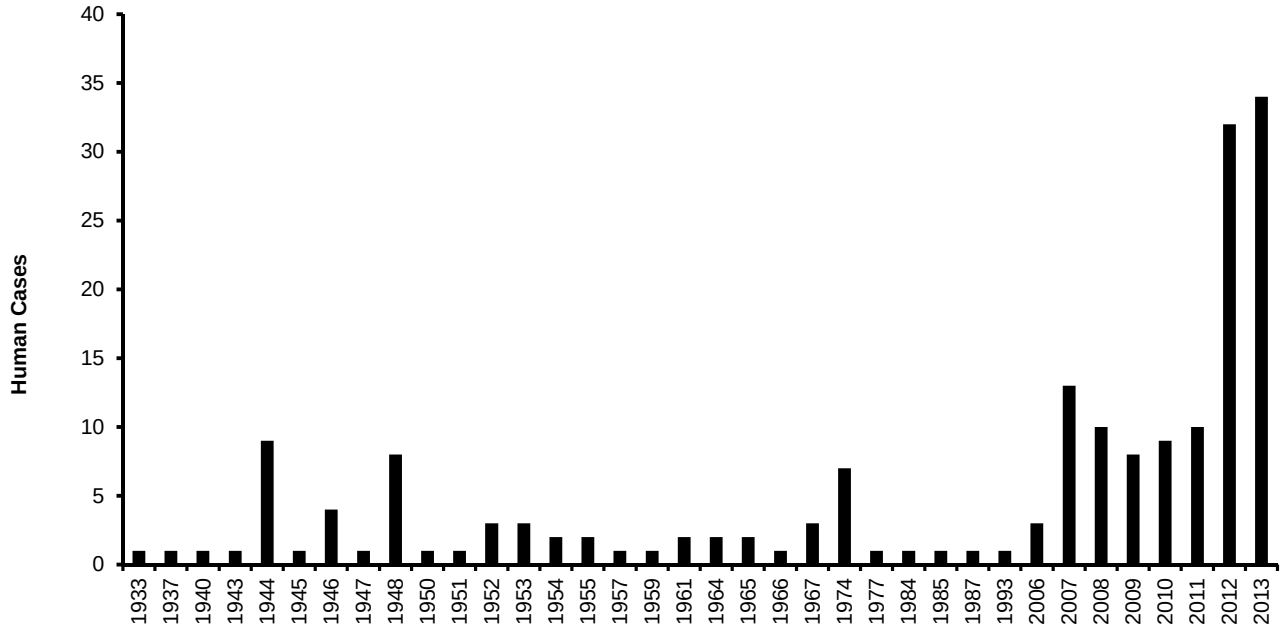

Figure 1. Historical and current suspected, probable, and confirmed human cases of flea borne typhus in Orange County, CA, 1933 - 2013.

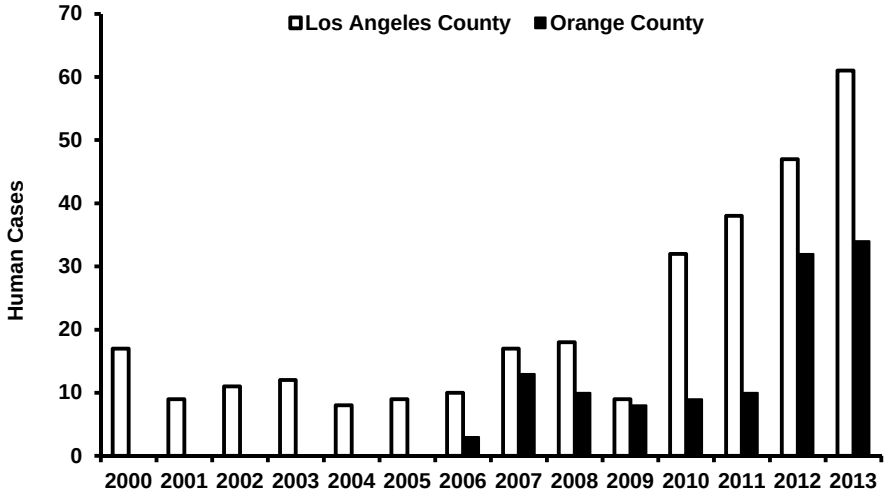

Figure 2. Human cases of flea-borne typhus in Los Angeles and Orange Counties, CA, 2000 - 2013.

STUDY AREA

Orange County occupies a large portion of the Greater Los Angeles Basin, and has an estimated population of 3,114,363 people living in a mostly metropolitan area of 790.6 square miles; the population density is approximately 3,942 persons per square mile and is the third most populous county in the state (U.S. Census Bureau 2014). Most of Orange County's population lives in two coastal, urbanized areas of the Santa Ana and Saddleback Valleys. The region's climate is Mediterranean, moderated by easterly winds from the Pacific Ocean, with a mean annual rainfall of 13.59 inches and a mean annual temperature of 64.55°F. (OC Weather 2014). The weather is typically warm and dry from May - October, with precipitation occurring mainly during November - April.

COMPONENTS OF THE ORANGE COUNTY VECTOR CONTROL DISTRICT'S FLEA-BORNE TYPHUS PROGRAM

In response to the increasing disease burden, the Orange County Vector Control District (District) established a flea-borne typhus prevention and response program after the initial outbreak in 2006. The District has also participated in joint studies with the Centers for Disease Control and Prevention (CDC), and with the Bacterial and Rickettsial Diseases Laboratory at the Walter Reed Army Institute of Research (WRAIR), and began collecting more data regarding animal hosts and their exposure to infective fleas. District staff obtained scientific collecting permits from the California Department of Fish and Wildlife (CDFW) to collect and sample small mammals, and adhered to animal euthanasia protocols per the American Veterinary Medical Association (AVMA) guidelines (AVMA 2007). The District has consulted with CDFW, local cities and their code enforcement departments, and the Orange County Animal Care (OC Animal Care) when feral cats are identified as possible contributors to a human case.

The District's flea-borne typhus prevention and response program consists of two main components: ecological investigations of human cases to determine neighborhood risk, and a public education program. Results from the ecologic investigation guide the geographic extent of the public education campaign.

Components of the Ecologic Investigation Include:

- Inspection for backyard wildlife – opossums, feral cats, raccoons, skunks, rats, and house mice (*Mus musculus*);
- Inspection for conditions conducive to infestations, such as harborage, food, and water sources;
- Inspection of companion cats and/or dogs for evidence of flea infestations;
- Inspection for evidence of flea infestations on property via "white sock" method (Borchert et al. 2012);
- Trapping of opossums to determine the flea index (# fleas/animal) as an indication of neighborhood risk. The District surveyed opossum populations by setting animal traps (Tomahawk Live Trap, Hazelhurst, WI) near flea-borne typhus exposure sites. Trapped opossums were processed according to AVMA guidelines (AVMA 2007);
- Testing of fleas and animal specimens via qPCR (Eremeeva et al. 2012) and/or serology (Fogarty et al. 2013) to determine the rickettsial infection rate in vectors and host animals.

Components of the Public Education Campaign Include:

- Notification of residents geographically contiguous with the presumed exposure site (neighborhood notification, door-to-door campaign). The extent of the neighborhood notification is dependent on the flea index and total number of opossums trapped at the exposure site. If the flea index exceeds historical averages, the area surrounding the exposure site is expanded for the neighborhood notification (door-to-door) education campaign. District Inspectors visit properties surrounding the exposure site and provide residents with information about flea-borne typhus and offer inspections of properties for conditions conducive to backyard wildlife;
- Posting notifications of flea-borne typhus activity on signs and light posts throughout the defined public

education campaign area for two weeks during the ecologic investigation;
- If conditions are conducive to backyard wildlife, District personnel educate residents on ways to make their properties less attractive to these animals. Residents are advised to put their pet animals on flea control and/or contact a structural pest control company for environmental flea control. If necessary, topical flea control is provided to homeowners in the area surrounding human cases.

RESULTS OF ECOLOGIC INVESTIGATIONS

Flea Infection Rate

During a collaborative study with CDC, 727 batches (i.e., pools) of *C. felis* (approximately 2 fleas/pool, n=1,405 total fleas) were collected from 2007-2008 and later tested by qPCR. Of these, 58.9% tested positive for *R. felis*, while only 7 pools (0.9%) were found with *R. typhi*; other flea species were collected at insignificant levels and showed little evidence of rickettsial infection (Eremeeva et al. 2012). Of a small number of *C. felis* (n=56) collected from 6 companion cats from human flea-borne typhus case homes and analyzed in 29 pools, 22 pools (75.9%) tested positive for *R. felis*, suggesting the importance of domestic cats as transport hosts of fleas to humans (Eremeeva et al. 2012).

Opossum Flea Index

In total, 259 opossums were evaluated from 2006-2013, yielding 23,531 fleas. The average flea index was determined to be approximately 91 fleas/opossum (range 0-726 fleas/opossum). The number of opossums trapped at flea-borne typhus exposure sites ranged between 0-24 opossums. Since skunks, raccoons, rats, and house mice are not considered important reservoirs for flea-borne typhus in southern California because of their relatively low flea load (Adams et al. 1970, Schwan et al. 1985, Sorvillo et al. 1993), they were released at the capture site and not included in the study.

Animal Infection Rate

In total, 81 tissue samples from 16 opossums were examined, and 4 animals tested positive for *R. felis* via qPCR (Eremeeva et al. 2012). In a separate serological study, Fogarty et al. (2013) found that 41.6% (84/202) of sampled opossums were serologically positive for *R. typhi* antibodies. Although the ELISA used in the study could not distinguish between *R. felis* and *R. typhi* antibodies, it did indicate the extent of rickettsial infection in the opossum population.

Exposure Sites of Human Flea-borne Typhus Cases

From 2012-2013, 66 detailed case site investigations were made. Approximately 85% (56/66) of the cases reported seeing backyard wildlife, such as opossums, raccoons, skunks, and feral cats, around the case homes. Approximately 77% (51/66) of the cases self-reported owning pets, primarily domestic dogs and/or cats, with one case owning an opossum; 27% (18/66) of cases reported exposure to a rescued cat, cared for a cat colony, adopted strays, or had a cat colony at their worksite. Nearly 65% (43/66) of the cases reported seeing opossums on their property, with 3 cases having removed a dead opossum from their yard. Additionally, 3 victims reported performing landscaping/brush removal on their property prior to illness onset, and 4 exposure sites produced fleas off human baits. Finally, 7 cases claimed that they had no animal exposure: they did not own pets or notice backyard wildlife around their residences, suggesting that exposure to fleas occurred in the community.

Human Cases

The Orange County Health Care Agency (OC Health Care) provided epidemiologic assessments on 109 flea-borne typhus cases that occurred in the county from 2006-2013. Approximately 58% (63/109) of the victims were male, the median age of the cases was 44 years, and 16% (17/109) of the cases were under 18 years of age. Altogether, 85% (92/109) of the patients required hospitalization, with a median length of stay of 5 days (range 1-368 days). Disease transmission likely occurred at the place of residence for 87% (61/70) of the victims, and when asked, only 26% (17/65) of the cases recalled an insect bite prior to disease onset. Human flea-borne cases occurred year-round but in a bi-modal distribution, with July (17 cases) and December (15 cases) as the most active months. Geographically, all cases in Orange County occurred in highly populated urban areas in the northern half of the county, while none occurred in the rolling foothills of south county.

DISCUSSION

Since zoonotic diseases are inherently complex, a key question in disease ecology is how to mitigate pathogen transmission from free-roaming and abundant animal reservoirs to human populations (Salkeld et al. 2013). Flea-borne typhus is an example of a zoonotic disease that is difficult to manage from a public health perspective, since transmission is so closely associated with humans and backyard wildlife, feral cats, companion animals, and an abundant vector, the cat flea. Our data showed that nearly 77% of victims reported owning a pet cat or dog or were involved in the care of feral cats. In addition, 65% of cases reported seeing opossums, a common peridomestic animal frequently infested with cat fleas.

Although the causes for the recent increase in human flea-borne typhus cases in the affected southern California counties are not well-defined, this rise has been accompanied by changes in how public and privately-sponsored animal control groups manage nuisance animal populations, especially opossums and feral cats, the two important hosts for the cat flea. The passage in 1998 of California's Hayden Law (SB 1785, Chapter 752, Statutes of 1998) required animal control agencies to end the euthanasia of adoptable and treatable animals by 2010, especially of unwanted cats. Today, most animal services focus on animal rehabilitation/adoption/rescue through partnerships with animal rescue groups, rather than control.

With ample food and harborage available in suburban neighborhoods, opossums have increased throughout the state after introduction in 1910 (Grinnell 1915). For many years, OC Animal Care routinely euthanized

opossums (approximately 3,000/yr) whenever the public submitted an animal for disposal as nuisance wildlife, but opposition by the Opossum Society of California eventually led in 1988 to the end of euthanasia of healthy opossums in Orange County. Currently, OC Animal Care processes only injured, sick, or dead opossums or opossums that have been involved in a bite with a human, and they will refuse acceptance of healthy opossums trapped by the public (OC Animal Care 2014a). Although CDFW regulations prohibit the relocation of wildlife (Title 14 CCR Sect. 465.5), many residents and rescue groups have relocated nuisance opossums to other neighborhoods on their own as a matter convenience. In some instances, the inadvertent relocation of opossums from typhus endemic to non-endemic areas by well-meaning individuals or groups may have contributed to the spread and amplification of this disease in Los Angeles County (J. Ramirez, pers. commun.).

One issue the District has recently been faced with is the role that OC Animal Care has taken regarding feral cats. Unlike dogs, cats are allowed to roam freely and are not required to be licensed in Orange County, resulting in large populations of feral cats and kittens. In an attempt to reduce the free-roaming cat population, OC Animal Care implemented its Feral FREE program in 2014 with $110,000 in combined grant money from the ASPCA ($50,000), PetSmart Charities ($50,000), and Petco Foundation ($10,000) (OC Community Resources 2014). The Feral FREE program uses Trap-Neuter-Return (TNR) as the method of choice to reduce shelter intake and euthanization rates of unadoptable cats. In the program's TNR, healthy but unadoptable feral cats are sterilized, vaccinated for rabies, and returned to the communities they come from by volunteers with Feral Alley Cats and Friends of SPCA. Within the first year of implementation, over 1,400 unadoptable cats have been spayed/neutered and released back in the communities, resulting in a 24% decline in the rate of cat euthanization (OC Animal Care 2014b). In 2013, OC Animal Care euthanized 74% (8,944/12,084) of the cats submitted to the shelter; this action comprised the highest percentage of the agency's euthanasia and costs (OC Animal Care 2014b).

While TNR may be a comfortable solution for animal control agencies, the District believes that OC Animal Care's Feral FREE program will negatively affect public health and put residents at increased risk of coming into contact with fleas carrying flea-borne typhus. OC Animal Care, as a governmental agency, should consider the threat to public health and legal liabilities posed by releasing hundreds of animals capable of harboring infected fleas in an area where flea-borne disease is endemic. The District has requested that the Feral FREE program be subjected to the California Environmental Quality Act (CEQA) process and receive a full environmental impact analysis. The review should also state the objectives of the Feral FREE TNR program and methods and variables used to analyze the effectiveness of the program. Because the efficacy of similar TNR programs in the United States are highly debatable (Longcore et al. 2009) and is opposed by CDFW (CDFW 2014), the analysis of the program should be able to withstand scientific scrutiny. The Feral FREE program should also include a plan to monitor and manage cat colonies created by the program. As regards to a long-term solution, the District supports establishment of a cat licensing program in the county.

OC Animal Care has not agreed to the District's request for a CEQA review and maintains that all CEQA requirements have been explored by the County's planning division. The reviewers believe that the Feral FREE program does not qualify as a "project" and that there will be no significantly-adverse environmental impacts or need to mitigate aspects of the TNR. Since returned cats will be released only in the neighborhoods from which they originated, the program will not be adding new cats to existing populations. According to OC Animal Care, no cities objected to its Feral FREE TNR program. Additionally, city code enforcement entities have no authority to regulate free-roaming cats.

OC Animal Care has agreed to a request by the District not to release cats to areas less than 0.3 miles from County of Orange workplaces, schools, parks, or health care facilities, areas with a geographic cluster of human flea-borne typhus cases as determined by the OC Health Care Agency, mobile home parks, areas with an established feral cat colony, and to disclosure the release sites. The Feral FREE program, however, uses a flea treatment that lasts only 30 days, which precedes the spay/neuter surgery. This means that less than 30 days after the cats are returned to the community, they can once again harbor flea infestations that are potentially infected with flea-borne typhus: the more fleas on a property, the greater risk to humans.

The District is working with OC Animal care to develop a transparent and comprehensive review of the Feral FREE program. OC Animal Care is assisting the District in its public awareness campaign by distributing flea-borne typhus education materials while the Feral FREE program is being analyzed. The public health obligation for which governmental animal control agencies were created and the importance of their role in animal management must be emphasized as one way to prevent outbreaks of flea-borne typhus.

The District will continue to make every effort to protect the people of Orange County from vector-borne disease. The District's main strategy of preventing flea-borne typhus consists of making people aware of the risks and the steps they can take to avoid contracting the disease. The key to prevention of flea-borne typhus is to limit the public's exposure to potentially infected fleas. The District strives to:

- educate people about the importance of maintaining household pets on a flea control program to break the vector bridge to the human population;
- inform governmental agencies and community groups to discourage feeding of wildlife and the creation of cat colonies;
- educate the public on the disease risks associated with opossums, feral cats, and fleas.

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