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Fleas as Vectors of Emerging Zoonoses

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Abstract

As blood-feeding insects, fleas are vectors of bacteria, such as *Yersinia pestis*, *Rickettsia felis*, *Rickettsia typhi* and *Bartonella henselae*, as well as viruses, such as the feline leukemia virus (FeLV). Fleas are also intermediate hosts for the parasitic larval stadia of the dog and cat tapeworm, *Dipylidium caninum*. The most important current emerging flea-borne zoonotic diseases are the cat-scratch disease, caused by *B. henselae* and the flea-borne spotted fever caused by *R. felis*. Pathogen transmission by fleas takes place in many ways. Fleas are not host-specific and feed on many different hosts, such as humans, and transmission of pathogens may occur through these flea bites. Further transmission to humans can also occur via certain reservoir hosts, which are usually companion animals. This review presents information on the emergence of flea-borne zoonoses, including flea biology, life cycle and transmission modes. Additionally, prevention and control of flea-borne pathogens is outlined, including flea control failure in the environment.

Keywords

Fleas, Arthropod Vectors, Zoonoses, Communicable Infectious Diseases, *Bartonella Henselae*, *Rickettsia Felis*

PULGAS COMO VECTORES DE ZOONOSIS EMERGENTES

Resumen

Las pulgas, como insectos que se alimentan de sangre, son vectores de bacterias, como *Yersinia pestis*, *Rickettsia felis*, *Rickettsia typhi* y *Bartonella henselae* y virus, como el virus de la leucemia felina (FeLV). Las pulgas son huéspedes intermediarios en estadios larvarios de la tenia del perro y el gato *Dipylidium caninum*. Las zoonosis emergentes transmitidas por pulga más importantes actualmente son la enfermedad por arañazo

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de gato causada por *B. henselea* fiebre manchada transmitida por pulga causada por *R. felis*. La transmisión de patógenos por las pulgas se lleva a cabo de muchas maneras. Las pulgas no son un huésped específico y se alimentan de muchos huéspedes diferentes, como el ser humano, y a través de estas picaduras de pulgas la transmisión de patógenos puede ocurrir. La transmisión a los seres humanos pueden también ocurrir a través de ciertos reservorios, que suelen ser animales de compañía. Esta revisión presenta información sobre la emergencia de las zoonosis transmitidas por las pulgas, incluyendo la biología de la pulga, ciclo de vida y modos de transmisión. Además, se describe la prevención y el control de los patógenos transmitidos por las pulgas, incluyendo la fallas de control de pulgas en el ambiente.

Palabras clave

Pulgas, artrópodos vectores, zoonosis, enfermedades infecciosas, *Bartonella Henselae*, *Rickettsia Felis*.

PULGAS COMO VECTORES DE ZONOSIS EMERGENTES

Resumo

As pulgas, como insetos que se alimentam de sangue, são vetores de bactérias, como *Yersinia pestis*, *Rickettsia felis*, *Rickettsia typhi* e *Bartonella henselae* e vírus, como o vírus da leucemia felina (FELV). As pulgas são hospedeiros intermediários dos estádios larvares da tênia do cão e do gato *Dipylidium caninum*. As zoonoses emergentes mais importantes transmitidas por pulgas atualmente são a doença da arranhada do gato causada por *B. henselea*, a febre manchada, transmitida pela pulga causada por *R. felis*. A transmissão de patógenos por pulgas é levada a cabo de várias formas. As pulgas não são um hospedeiro específico e alimentam-se de muitos hospedeiros diferentes, como o ser humano e a transmissão de patógenos pode ocorrer através desta picada de pulga. A transmissão aos seres humanos pode também ocorrer através de certos reservatórios que podem ser animais de companhia. Esta revisão apresenta informação sobre a emergência das zoonoses transmitidas por pulgas, incluindo a biologia da pulga, ciclo de vida e modos de transmissão. Para além disso descreve-se a prevenção e controle dos patógenos transmitidos por pulgas incluindo as falhas de controle das pulgas no ambiente.

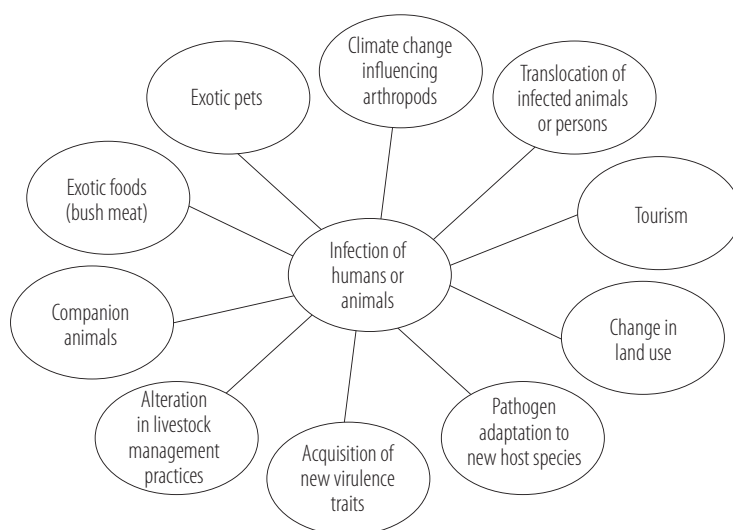
Palavras chave

Pulgas, artrópodos vectores, zoonosie, enfermidades infecciosas, *Bartonella henselae*, *Rickettsia felis*

Introduction

Fleas are important vectors of several pathogens, and transmission takes place in many different ways. The majority of these pathogens are zoonotic (Parola *et al.*, 2005). Nowadays there are many companion animals worldwide living in a close relationship with humans. Transmission of pathogens to humans is likely, especially when these companion animals are heavily infested by fleas.

Figure 1. Factors influencing new and reemerging zoonoses



Source: Cutler *et al.* (2010)

Approximately 15 years ago, zoonotic pathogens such as *Rickettsia felis* and *Bartonella henselae* were isolated for the first time and ever since then an increasing number of infections caused by these pathogens have been reported worldwide. These pathogens are considered to be emerging (Otranto & Wall, 2008; Beugnet & Marie, 2009). An emerging zoonosis is caused by a pathogen that is recognized or evolved for the first time, or re-introduced and which causes an increase in epidemiology (geographical distribution, incidence, prevalence and pathogenicity). There are many factors that influence the epidemiology of flea-borne zoonotic pathogens (Figure 1). In recent years, animal transportation and pets travelling with their owners has increased. In this way, infected fleas on animals could be introduced in different parts of the world, which increases

infection risk in both animals and humans. Landscape changes create harbor niches for peri-domestic hosts. These hosts are necessary to maintain an infection in the flea population. Climate changes are responsible for a more widespread distribution of fleas, as fleas reproduce better in warm and humid climates. Seasonal change may reduce the winter period so that fleas can be active all year. Moreover, pathogens can adapt to new host species, for example other arthropods, for wider distribution (Beugnet & Marie, 2009; Cutler *et al.*, 2010). The aim of this review is to give an overview of flea-borne emerging zoonoses worldwide, based on flea biology, the flea's life cycle and the transmission modes.

Flea Biology

Fleas (Siphonaptera) are small, obligate, blood-feeding insects without wings. There are about 2,500 flea species and, morphologically, they are very similar. Fleas are vectors and are able to transmit a variety of pathogens in and between animal species, as most flea species are host-preferential for mammals (a few for birds) rather than host-specific. Flea species that are found mostly on cats and dogs worldwide are *Ctenocephalides felis*, *Ctenocephalides canis*, *Pulex irritans*, *Archaeopsylla erinacei*, *Spilopsyllus cuniculi*, *Echidnophaga gallinacea* and *Xenopsylla cheopsis* (Akuczewich *et al.*, 2002; Alcaïno *et al.*, 2002; Durden *et al.*, 2005; Beck *et al.*, 2006; Bond *et al.*, 2007; Rinaldi *et al.*, 2007; Gracia *et al.*, 2008; Changbunjong *et al.*, 2009; Farkas *et al.*, 2009). These flea species are associated to certain pathogens that may cause diseases in humans (Table 1).

Table 1. Flea species, their pathogens, transmitted diseases in animals and humans, and their geographical distribution

Flea species	Geographical distribution (flea species)	Pathogens		Disease	Geographical distribution (diseases)
<i>Ctenocephalides</i> spp.	Worldwide	Bacteria	<i>Bartonella</i> spp. <i>Rickettsia typhi</i> <i>Rickettsia felis</i>	Bartonellosis* Murine typhus* Flea-borne spotted fever*	Worldwide Worldwide Worldwide
		Viruses	<i>Feline leukemia virus</i>	Feline leukemia**	Worldwide
		Helminths	<i>Dipylidium caninum</i>	Dipylidiosis*	Worldwide

Flea species	Geographical distribution (flea species)	Pathogens		Disease	Geographical distribution (diseases)
<i>Pulex irritans</i>	Worldwide, but now uncommon in the U.S.A. and most of northern Europe	Bacteria	<i>Yersinia pestis</i> <i>Bartonella rochalimae</i> <i>Rickettsia felis</i>	Plague* Bartonellosis* Flea-borne spotted fever*	Worldwide Worldwide? Worldwide
<i>Archaeopsylla erinacei</i>	Europe, North America	Bacteria	<i>Rickettsia felis</i>	Flea-borne spotted fever*	Worldwide
<i>Spilopsyllus cuniculi</i>	Worldwide	Virus Bacteria	<i>Myxoma virus</i> <i>Bartonella alsatica</i> <i>Rickettsia felis</i>	Myxomatosis Bartonellosis* Flea-borne spotted fever*	North and South America, Europe, Australia Worldwide Worldwide
<i>Echidnophaga gallinacea</i>	Tropical, subtropical and temperate areas, now also in North America	Virus Bacteria	<i>Fowl poxvirus</i> <i>Yersinia pestis</i> <i>Rickettsia felis</i>	Fowl pox Plague* Flea-borne spotted fever*	Worldwide? Worldwide Worldwide
<i>Xenopsylla cheopis</i>	U.S.A., South America, Europe, Africa, Asia	Bacteria	<i>Yersinia pestis</i> <i>Bartonella elizabethae</i> <i>Rickettsia felis</i> <i>Rickettsia typhi</i>	Plague* Bartonellosis* Flea-borne spotted fever* Murine typhus*	Worldwide Worldwide? Worldwide Worldwide

* Zoonotic disease.

** Potential zoonotic disease.

Source: The authors

C. felis, the cat flea, is the most common flea found on cats and dogs worldwide (Dryden & Rust, 1994; Rust & Dryden, 1997; Taylor *et al.*, 2007). Most cats are more infested than dogs, probably because of their roaming activities. *C. canis* is the dog flea and very similar to *C. felis*. Domestic dogs are more likely to be infested by *C. felis*, but dogs in kennels and in rural areas are more likely to be

infested by *C. canis*. *P. irritans* is the human flea and can be found on humans, dogs, cats, rats, and badgers, and is most commonly found on pigs and in farming areas. *A. erinacei* is the hedgehog flea; it is hosted by hedgehogs, dogs and cats, and it may be transferred from hedgehogs through direct contact. *S. cuniculi* is the European rabbit flea and the hosts are rabbits, hares, dogs and cats. Dogs and cats are infested by hunting and frequenting rabbit habitats. *E. gallinacea* is the stick tight flea and can be found on poultry and birds, but it can also attack dogs, cats, rats, rabbits, horses, humans and larger insectivores. *E. gallinacea* can survive off-host, mostly indoors and in beddings (Taylor *et al.*, 2007). *X. cheopsis* is the oriental rat flea (Wimsatt & Biggins, 2009); its reservoir hosts are rodents, small ruminants and domesticated animals like dogs, cats, rabbits and rats (Koutinas *et al.*, 1995; Ibrahim *et al.*, 2006; Amatre *et al.*, 2009; Eisen *et al.*, 2009).

The most relevant flea species is the *C. felis*. This flea species is the most common one and has been detected on over 50 different host species worldwide. Moreover, it is a vector with a wide range of pathogens and plays an important role in the transmission of certain (emergent) zoonotic diseases (Taylor *et al.*, 2007; Otranto & Wall, 2008).

Life Cycle of the Flea

The life cycle of the *C. felis* has 4 main stages: eggs, larvae, pupae and adults (Rust & Dryden, 1997; Dryden *et al.* 2000). Only the adults, males and females, are blood feeders. The duration of the total life cycle depends on environmental conditions, but ranges from a couple of weeks to several months (Taylor *et al.*, 2007).

Eggs

Females begin to oviposit between 24 and 48 hours after blood feeding. Eggs may be laid on the host or on the ground and soon they will drop onto substrates, where hatching occurs. Usually, eggs will accumulate in sleeping or resting sites where pets frequently reside. In optimal environmental conditions, females may oviposit about 30-50 eggs per day on average. The optimal environmental conditions depend on temperature and humidity and eggs cannot withstand major environmental changes. Hatching will usually occur in 1 day to 2 weeks (Dryden & Rust, 1994; Rust & Dryden, 1997; Taylor *et al.*, 2007).

Larvae

After hatching, larvae consume the eggshells. For optimal larval development, they need adult flea feces with dried blood. Larvae are also cannibalistic; they feed on other larvae (Taylor *et al.*, 2007). Larvae are negative phototactic and positively geotactic and will usually burrow into carpets in homes. In order for full maturity to occur, larvae need a relatively moist air or soil and no extreme temperatures.

Pupae

After spinning a cocoon by emptying its gut, the mature larva develops into a pupa. The process of spinning a cocoon requires a vertical surface that they can focus on. Cocoons are present in soil, on vegetation, in carpets, under furniture and on sleeping or resting sites for pets. When the pupal stage is disturbed after completing the cocoon, the larva will leave the cocoon and spin a second one or develop as a naked pupa. The duration of the pupal stage ranges from 8 to 9 days when temperature is 24°C and relative humidity is 78 percent. Of all immature stages, pupae are most resistant to desiccation (Dryden & Rust, 1994; Rust & Dryden, 1997; Taylor *et al.*, 2007).

Adults

Pupae develop into adults in the cocoon and they may remain within the cocoon for up to 140 days or even for up to 12 months (Taylor *et al.*, 2007). The cocoon has several functions; it serves as protection against predators and as a barrier to emergence. Emergence of adults is stimulated by mechanical pressure and heat, which are particularly present when pets are lying down at their sleeping or resting sites. Emergence, however, is not stimulated by vibrations (Rust & Dryden, 1997). After emergence, adults begin to feed on the host as soon as possible. Adults produce feces within 10 minutes after blood feeding, which serves as nutrition for larvae. Females also mate with several males soon after emergence, within 36 hours (Taylor *et al.*, 2007). The female starts to produce eggs to complete the life cycle of *C. felis*.

Transmission of Flea-Borne Zoonotic Pathogens

Flea-Host Transmission

Transmission of flea-borne pathogens to hosts can occur in many ways. Fleabite is the best-known transmission route. Fleabites can cause direct damage to the host through excreting saliva, skin lesions, allergic reactions and blood loss. Besides, fleas can cause disease in their hosts through the transmission of pathogens. Fleas can also cause damage indirectly (Otranto & Wall, 2008). Fleas are subsequently present on the host's fur. Aside from feeding and producing eggs on the host, adult fleas also produce a certain amount of feces. Inoculation of flea feces takes place through scratching feces into skin lesions, caused by fleabites or already existing skin lesions. Hosts can also inoculate flea feces and/or adult fleas by grooming (Chomel *et al.*, 1996).

Flea Infection by Pathogens

Pathogens depend on transmission to new hosts in order to survive on a long-term. Pathogen fitness and transmission mode are important for the infection of new healthy hosts to succeed (Bosch *et al.*, 2010). Primary flea infection probably takes place through close contact between fleas and pathogens in the environment or during blood feeding on infected hosts. Infected fleas can spread the infection in the flea population through vertical and/or horizontal transmission. Horizontal transmission takes place between infected and uninfected fleas. The route of transmission is probably by co-feeding. Through transmission of a pathogen in saliva or regurgitation, an infected flea would be able to infect uninfected fleas feeding nearby. Another transmission route is by larval feeding, in which transmission of pathogens to uninfected larvae is facilitated by feeding on infected flea feces and/or cannibalism of infected eggs/larvae. Vertical transmission of pathogens is achieved by flea reproduction. Vertical transmission is through transstadial and transovarial transmission, as described for *R. felis* (Reif & Macaluso, 2009).

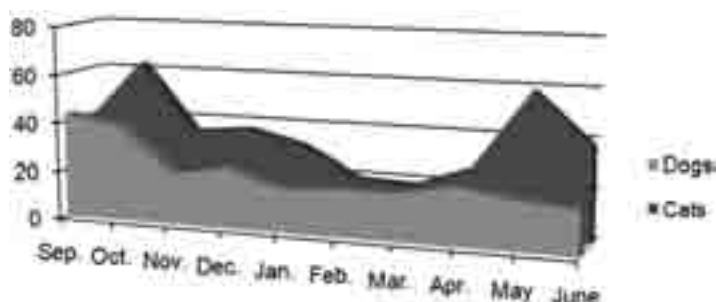
Reservoir Hosts of *C. Felis*

Fleas are associated with a wide range of hosts worldwide. *C. felis* can be found on cats and dogs and other animals such as domestic rabbits, horses, cattle, sheep, goats, jackals and poultry. Wild animals that may be infested are coyotes, red

and gray foxes, bobcats, panthers in Florida, skunks, raccoons, opossums, ferrets, mongooses, koalas and various rodent species. Companion animal reservoir hosts are mainly cats and dogs who live in close contact with their owners (Rust & Dryden, 1997).

Many studies have reported the prevalence and infestation of *C. felis* in dogs and cats, but there are not many seasonal studies regarding the flea prevalence. The flea infestation of *C. felis* in the west of France throughout the year is shown in Figure 2. The diagram shows that *C. felis* is found on dogs and cats all year round, with peaks in early autumn (September, October) and late spring (May, June) (Bourdeau & Blumstein, 1995). Seasonal prevalence of fleas has also been reported by other authors (Rust & Dryden, 1997; Beck *et al.*, 2006; Taylor *et al.*, 2007) when conditions of larval development are most favorable.

Figure 2. Flea infestation of *C. felis* in cats and dogs throughout the year



Source: Bourdeau & Blumstein (1995)

Humans as Accidental Hosts

Adult fleas are able to survive off-host and when fleas heavily infest companion animals, humans can get bitten. Naimer *et al.* (2002) reported cases of 20 patients with fleabite eruptions. In adults, stings were mainly concentrated on the legs and in children mostly on the arms, thorax and neck area. Fleabites eventually appeared as a central papula with erythema and intense pruritis. This skin reaction, papula urticaria, often develops after fleabites as a hypersensitivity reaction (Naimer *et al.*, 2002). Furthermore, fleas can cause disease in humans because they can transmit pathogens directly through their feeding habits (plague, flea-borne spotted fever) or indirectly via companion animals (cat-scratch disease).

Flea-Borne Zoonotic Diseases

Flea-Borne Zoonotic Pathogens

C. felis may be vector of bacteria (*Yersinia pestis*, *Bartonella henselae*, *Rickettsia typhi*, *R. felis*), viruses (retroviridae) and helminths (*Dipylidium caninum*). All these pathogens are geographically distributed worldwide (See Table 1) (Otranto & Wall, 2008). A wide range of *Bartonella* species are confirmed as potential human pathogens. Most of these are transmitted by arthropods, especially fleas (Chomel *et al.*, 2006; Billeter *et al.* 2008; Chomel & Kasten, 2010). *B. henselae* is the most important pathogen that causes cat-scratch disease and is described as a current emerging zoonosis.

R. typhi can cause murine typhus in humans. *R. felis* is a newly emerging zoonotic pathogen with *C. felis* as currently the only known vector (Reif & Macaluso, 2009).

The cysticercoid larval stage of *D. caninum* is transmitted by fleas, especially the *C. felis* and *C. canis* (Otranto & Wall, 2008). *D. caninum* is the dog tapeworm in canine and feline species and accidentally in humans, but human cases of *D. caninum* infection are rare (Otranto & Dantas-Torres, 2010).

Cats are reservoir hosts of feline retroviruses, which may be transmitted through bites, scratches, exposure to body fluids and needle injuries. Up to this moment there is no evidence that feline retroviruses are zoonotic. *C. felis* is a possible vector of *feline leukemia virus* (FeLV) and can transmit the virus horizontally (Vobis *et al.* 2003a; Vobis *et al.* 2003b). For other feline retroviruses like *feline immunodeficiency virus* (FIV) and *feline foamy virus* (FeFV), the transmission by vectors is unknown.

Y. pestis is the cause of the plague, a zoonotic disease with high morbidity and mortality. Accidental hosts are carnivores and humans (Wimsatt & Biggins, 2009).

Current Emerging Zoonoses

Current emerging flea-borne pathogens are *B. henselae* and *R. felis*. Infections caused by these pathogens in animals are called *bartonellosis* and *rickettsiosis* and in the human cat-scratch disease (CSD) and flea-borne spotted fever, respectively.

CSD was already described over 50 years ago in France, but *B. henselae* was only considered as the causative agent after the first isolation from domestic cats in 1992 (Boulouis *et al.*, 2005). *R. felis* was probably first discovered in cat fleas in 1918 (Parola *et al.*, 2005). It was later rediscovered in 1990, when a Rickettsia-like organism, that resembled *R. typhi*, was described (Adams *et al.*, 1990). In 1994 and 1995 this organism was isolated and given the name *Rickettsia felis* (Parola *et al.*, 2005).

Bartonellosis and Cat-Scratch Disease

Bartonellaceae are small, curved, Gram-negative bacteria. The preferred site of *B. henselae* in animals is in erythrocytes and endothelial cells. It is believed that the bacteria are also capable of infecting bone marrow progenitor cells. This way the infection persists in erythrocytes and in the infected animal's bloodstream.

B. henselae infection in cats has been reported worldwide, in both domestic and stray cats. The prevalence in domestic cats ranges from 10 to 40 percent (Iredell *et al.*, 2003). The cat flea is a competent vector in the transmission of *B. henselae* to cats. Direct cat-to-cat transmission among experimental infected kittens is not demonstrated (Chomel *et al.*, 1996). Cats are considered to be healthy carriers, as there are no major clinical signs of *bartonellosis* under natural conditions. When clinical signs do occur, lymphadenitis and gingivitis are the most frequently reported (Boulouis *et al.*, 2005). When cats are infected with FeLV or FIV, pathogenicity of *B. henselae* infection increases (Breitschwerdt, 2008). In experimental conditions, the clinical manifestations are fever, lethargy, anorexia, cutaneous lesions, stomatitis, kidney and urinary tract infections, reproductive disorders, endocarditis and neurologic dysfunction (Chomel, 2000; Boulouis *et al.*, 2005). Uveitis is also reported as a clinical sign (Kerkhoff *et al.*, 1999). Cats are usually bacteriaemic from weeks to months, but some for more than a year. Young cats and strays are more likely to be bacteriaemic than older cats and domestic cats (Chomel & Kasten, 2010). In a study by Zangwill *et al.* (1993), the prevalence of CSD in humans could be related to the type of contact between humans and kittens (scratching, biting, licking, sleeping with a kitten and combing a kitten).

Besides cats, dogs have also been reported to be infected by *B. henselae*. Dogs could probably play a role in the transmission of *B. henselae* to humans; however, further research is required (Chomel, 2000, Mexas *et al.*, 2002).

The role of dogs as a chronically bacteriaemic reservoir of *B. henselae* has not been determined and it is more likely that domestic dogs are accidental hosts of certain *Bartonella* spp. (Chomel *et al.*, 2006). Clinical abnormalities in dogs infected by *B. henselae* are described as granulomatous hepatitis, peliosis hepatitis, generalized pyogranulomatous lymphadenitis and endocarditis (Breitschwerdt & Maggi, 2009).

The prevalence of *B. henselae* infection in humans is worldwide (Chomel, 2000; Chomel *et al.*, 2006). CSD occurs in humans of all ages, although most of them are under twenty years old. Most infections are seen during autumn and winter, which is probably due to the high prevalence of *C. felis* during autumn (Chomel, 2000), or maybe to the presence of more young cats with their new owners. Domestic cats are the main reservoirs of *B. henselae* for humans. Transmission happens mainly through cat scratches or, less likely, cat bites (Chomel *et al.*, 2006). Cat claws can namely become contaminated by infected flea feces (Chomel *et al.*, 1996; Breitschwerdt, 2008). The presence of *B. henselae* in cat saliva has not been clearly documented. Direct transmission of *B. henselae* to humans by fleabites is considered, but it has not been proven experimentally (Chomel *et al.*, 2006). After a cat scratch or bite, a skin lesion appears in 3 to 10 days. The skin lesion evolves from a vesicle to a pustule and finally into a papule (Chomel, 2000). In humans with CSD, mainly a benign regional lymphadenopathy develops in one to three weeks after exposure and persists for a few weeks to several months. Other clinical manifestations frequently reported are fever, malaise and aching, and sometimes headache, anorexia and splenomegaly (Boulouis *et al.*, 2005). Common clinical manifestations in immunocompromised individuals are bacillary angiomatosis (BA) and hepatic peliosis (HP) (Lamas *et al.*, 2010). There are many other clinical manifestations of *B. henselae* infection in human beings, which are reviewed in Boulouis *et al.* (2005).

Rickettsiosis and Flea-Borne Spotted Fever

Rickettsiae are small, rod shaped, Gram-negative bacteria. The pathogenesis of *R. felis* is unknown, probably because of limited knowledge about *R. felis* biology. The only current known biological and primary vector of *R. felis* is the cat flea (Reif & Macaluso, 2009). *C. felis* probably plays an important role in transmitting the infection to wild animals, domesticated animals and humans (Perez-Ororio *et al.*, 2008). The maintenance of *R. felis* in flea populations is probably through vertical (transstadial and transovarial) transmission in the cat flea (Wedincamp &

Foil, 2002). Other transmission routes in the flea population are by co-feeding, larval feeding and feeding on infected feces and/or cannibalism of *R. felis* infected eggs/larvae (Reif & Macaluso, 2009).

The main reservoir of *R. felis* is the cat flea but vertebrate hosts could also serve as a reservoir, as fleas may acquire *R. felis* from these hosts (Azad *et al.*, 1997). Although horizontal transmission between arthropods has not been reported, occasional horizontal transmission may be needed to maintain *R. felis* in arthropod population (Weinert *et al.*, 2009). Hosts associated with *R. felis* infected cat fleas are cats, dogs, rodents, hedgehogs, opossums, horses, sheep, goats, gerbils and monkeys (Perez-Osorio *et al.*, 2008). Horizontal transmission of *R. felis* to vertebrate hosts is a potential route of transmission. Vertebrate hosts are likely to be infected by saliva of infected fleas produced during blood feeding (Reif & Macaluso, 2009). Although the presence of *R. felis* in flea salivary glands is determined, the presence of *R. felis* in flea saliva is unknown (Macaluso *et al.*, 2008). If *R. felis* is not present in flea saliva, other possible transmission routes are through ingestion of infected fleas or contact of damaged skin or mucosa with infected flea feces (Labruna, 2009).

Many reports about *R. felis* infection do not mention clinical features in cats. This is probably because infection in cats is subclinical. Besides, cats are commonly infested by *R. felis* infected cat fleas, but very few cats have been reported to have active *R. felis* infection (Hawley *et al.*, 2007; Bayliss *et al.*, 2009).

Rickettsia felis infection in humans has several names, such as the flea-borne spotted fever, cat flea typhus and *R. felis* rickettsiosis. Human cases of *R. felis* infection have been reported in 12 countries around the world (Reif & Macaluso, 2009). In these cases patients had contact with fleas or animals known to carry fleas (Perez-Osorio *et al.*, 2008). Fleabites of *R. felis* infected fleas may result in infection in humans. The horizontal transmission route is probably similar as described for vertebrate hosts. Dogs may also play a role in the transmission of *R. felis* (Nogueras *et al.*, 2009).

Clinical manifestations in humans are described as fever, fatigue, headache, generalized maculopapular rash, cutaneous lesion surrounded by a halo, enlarged and painful lymph nodes in the inguinal region, rash and/or eschar (Parola

et al., 2005). Other, more severe, clinical symptoms are also described (Zavala-Velazquez *et al.*, 2000; Pérez-Osorio *et al.*, 2008; Reif & Macaluso, 2009).

Prevention and Control of Flea-Borne Pathogens

Surveillance

Surveillance of the progress of flea-borne pathogens is needed to prevent an increase in the number of cases worldwide. Emerging zoonoses are currently reported and monitored by the World Organization for Animal Health (OIE) and the World Health Organization (WHO). A global animal surveillance system for zoonotic pathogens is needed to give early warning of pathogen emergence and provide opportunities to control outbreak of pathogens (Kuiken *et al.*, 2005). For the surveillance of flea-borne pathogens, continuous research in fleas is required for the identification and prevalence of pathogens. Besides, control of zoonotic pathogens in reservoir host is needed (Cutler *et al.*, 2010).

Flea Control

Preventive measures against fleas are required in order to control the number of fleas and flea-borne pathogens. Flea control can occur in various ways: control indoors, mechanical control, control outdoors, biological control and on-host control. Control indoors is achieved with insecticides and/or insect growth regulators (IGRs). IGRs are a group of chemical compounds that interfere with the growth and development of arthropods, but do not kill the arthropod directly. IGRs mainly act on immature stages of arthropods and flea eggs and immature stages are sensitive to the ovicidal activity in various IGRs (Taylor, 2001; Rust, 2005). Mechanical control can be achieved by vacuuming, which will remove most of the eggs, larvae and adult fleas. Control outdoors can be achieved with adulticides, but these are not licensed in most countries for this purpose. Biological control is an alternative way of outdoor control. Placing ants as predators of all stages of fleas except for the cocoon in the environment is a way of biological control. On-host flea control can be accomplished with insecticides, including shampoos, sprays, collars, dips, foams, powders, spot-ons and oral systemics (Rust & Dryden, 1997). Systemic and topical insecticides have been revolutionized for the past ten years, thus usually only treatment of animals is already effective enough (Rust, 2005). A combination of IGRs and insecticides in spot-ons provide for prolonged ovicidal activity, even when residual activity

of the insecticide is reduced (Rust & Dryden, 1997). With this combination, the development of insecticide resistance is considerably diminished, because the life cycle of the flea is disrupted in many different ways (Blagburn & Dryden, 2009). Monitoring systems are used to collect information about which flea populations are resistant to what insecticides. This information is available to researchers worldwide (Blagburn, 2000).

Owner Awareness and Treatment Compliance

A survey was performed in Hungary in order to determine flea prevalence in domestic cats and dogs, as well as the owners' awareness. The result of the survey was that most owners did not know that their pets were infested with fleas and that they were unaware of the fleas' capability to transmit diseases to both animals and humans (Farkas *et al.*, 2009). A survey performed in the UK also revealed that many pet owners were unaware of their pets' flea infestation and the development of fleas in their home environment (Bond *et al.*, 2007). It could also be that pet owners cannot afford to buy flea control products or that they may use cheaper products, which may be not efficient enough (Farkas *et al.*, 2009). Moreover, many flea control products should be administered frequently (once a month, once every 3 months, once every 6 months, depending on the product) to be efficient. Failure to control fleas could also be due to the inability of pet owners to adequately apply flea control products to their pets (Dryden *et al.*, 2000). Therefore, pet owners might not be properly informed about flea infestation in the environment, the life cycle of the flea, the need for frequent administration and how to apply insecticides correctly to their pets.

Discussion

The zoonotic pathogens *B. henselae* and *R. felis* are currently considered as emergent pathogens. In the USA, the prevalence of *B. henselae* infection in both humans and animals is relatively high (Iredell *et al.*, 2003). In the Netherlands, however, there are about 2,000 cases of CSD estimated every year. Therefore, the incidence of CSD in the Netherlands is relatively low (Bergmans *et al.*, 1997). This also applies to the incidence of *R. felis* infection. Despite the fact that *R. felis* is distributed all around the world, human and animal cases of *R. felis* infection are rare (Kamrani *et al.*, 2008; Labruna, 2009). Hence, the incidence of infection caused by these pathogens to this moment may not be as high as expected.

In this review, only fleas were mentioned as vectors of zoonotic pathogens. There are other vector-borne arthropods aside from fleas. Other reported vector-borne arthropods of *B. henselae* are ticks and stable flies (Chomel *et al.*, 2006). There are potentially other vectors of *R. felis*, as *R. felis* has been detected in ticks and mites (Choi *et al.*, 2007; Oliveira *et al.*, 2008). Nevertheless, fleas are the main vectors of these pathogens. *B. henselae* and *R. felis* have found an excellent reservoir host, as *C. felis* is common worldwide in both domesticated and non-domesticated animals. In addition, flea infestation can occur throughout the entire year. In many countries flea control outdoors is not licensed. In this way, *C. felis* is very difficult to control in the outer environment and remains the common reservoir. Therefore, flea control in homes of pet owners is very important. Failure to control fleas is often related to the development of insecticide resistance, but development of insecticide resistance does not always have to occur. With the development of more flea control product combinations, development of resistance against these products is considerably diminished (Blagburn, 2000; Blagburn & Dryden, 2009). Pet owners are more likely to be unaware of their pets' flea infestation. Moreover, perhaps pet owners cannot afford flea control products or do not administer flea control products frequently (Farkas *et al.*, 2009). Hence, it is a great task for veterinarians and pharmaceutical industries to make pet owners aware of flea infestation in their homes and the consequences it may bring.

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