Bartonella and other plagues – New insights on fleas

Cutting-edge information brought to you by the CVBD® World Forum
Introduction

When Bayer HealthCare, Animal Health Division, called for the 1st International CVBD® Symposium in 2006, it was the first and initial step to address the global threat of canine vector-borne diseases (CVBD®). This was based on the belief that vector-borne diseases of the dog should be treated as one topic and dealt with on a global level and in an interdisciplinary way. During the past years, CVBD® have become a global issue and even sparked public interest. Many of the parasite-transmitted diseases affect humans as well as animals. The dog as man’s best friend plays an important role – being affected to a high extent by and serving as a host for some of the zoonotic pathogens.

At the first symposium, the participants agreed to form the CVBD® World Forum. Besides gathering knowledge, the main task for this group of international experts has been to raise awareness for the specific regional risks of CVBD® and to foster preventative measures. For this reason, the CVBD® World Forum created a website (www.cvbd.org) to provide the veterinary practitioner with cutting-edge and clinically relevant scientific information on CVBD®.

In CVBD® Digest, relevant findings from CVBD® symposia are presented periodically to veterinary practitioners. “Old-fashioned” fleas have gained interest since new emergent pathogens like Bartonella bacteria have been identified that use them as a vector. And knowledge about Bartonella spp. is still scarce in veterinary medicine. A further important aspect is public health, as cat and dog fleas may be shared between pets and their owners. Many pet owners are unaware of the rapid and synchronous breakdown of pre-emerged adult fleas on presentation of a suitable host after absence of hosts, e.g., during the winter pause. Moreover, fleas transmit numerous zoonotic pathogens, where dogs and cats function as reservoirs.
Fleas are cosmopolitan ectoparasites with a large variety of hosts. For companion animals and humans, the cat flea *Ctenocephalides felis* and the dog flea *C. canis* represent the most important species worldwide. Apart from causing flea allergy dermatitis (FAD), the ability of fleas to function as vectors for disease pathogens, such as *Bartonella* spp., is gaining more importance. Besides the well-known human aspects of dermal irritation and hygiene, some of these infectious diseases also have a public health implication. Consequent flea control with highly efficient ectoparasiticides supports prevention of the direct effects of flea infestation on the pet and reduces the risk of transmission of flea-borne diseases to both pets and humans.

**Flea morphology and biology**

Fleas possess a history of about 60 million years and were already found on prehistoric mammals. Approximately 95% of the more than 2,000 described species and subspecies parasitize mammals, while the remaining 5% live on birds. The flea developmental cycle can be completed in as little as 14 days or last up to 140 days, depending mainly on temperature and humidity. For most flea species, these cycles are characterized by three events: the hatching of the egg, the period from 1st instar to pupa, and the period from pupa to adult (see Figure 1). The number of eggs laid by female fleas depends among other factors on grooming activities of the host, the host’s physiology and hormones in the peripheral circulation. There are reports of 11–46 eggs per day and up to well over 2,000 eggs over 113 days in unconfined fleas and cats restricted from grooming. After the egg hatches, the larva of cat and dog fleas passes through three larval instars within protected microhabitats inside or outside of dwellings that combine moderate temperatures, high relative humidity and a source of nutrition in the form of adult flea fecal blood. The late instar larva moves to an undisturbed place and spins a silk-like cocoon, in which it pupates, that with time becomes coated with dust and debris. The final pupal stage is the pre-emergent adult, which has completed its final moult, but remains within the cocoon for varying lengths of time. Pressure and heat act as indicators of a potential host and can determine the length of the pupal stage. This can occur after approximately ten days or for up to six months in the case of the pre-emerged adult. The so-called pupal window may compromise control measures and has to be explained to pet owners. In its final stage, the adult flea begins seeking a host almost immediately after emergence. The survival time of unfed adult fleas ranges from 20 to 62 days, depending on the surrounding climatic conditions. After the first blood meal, fleas must continue to feed and reproduce in order to keep their metabolism in balance. The amount of blood consumed by a female cat flea averages 13.6 µl (± 2.7 µl) per day, which is equivalent to ~15 times its body weight.
The survival and longevity of adult fleas on a host is strongly influenced by the grooming behavior of the flea-infested animal. Restriction of grooming activity has allowed survival of cat fleas on hosts for at least 133 days.

Species diversity and distribution

The more than 2,000 described species and subspecies of fleas throughout the world mostly belong to the families Pulecidae and Ceratophyllidae. For relevant representatives of both families including respective hosts (dogs and cats) see Table 1. In general, the species *Ctenocephalides* with its representatives *C. felis felis* and *C. canis* both occur worldwide and are the most important flea species parasitizing dogs and cats.

The cat flea *C. felis* (see Figure 2) has formerly been divided into four subspecies: *C. felis felis* (worldwide distribution, from warm tropical areas to temperate zones with prolonged subfreezing temperatures), *C. felis orientis* (Southeast Asia and the East Indies), *C. felis damarensis*, and *C. felis strongylus* (both restricted to Africa), the latter two of which have more recently been proposed as full species. *C. felis felis* is often only referred to as *C. felis*, also from this point throughout this article.

Clinical signs of flea infestation

Apart from a number of pathogens for which the flea is a potential vector and which may also cause diseases on their own (see below), dermatological disorders in small animals caused directly and indirectly by fleas, probably outnumber all other dermatological disorders of different etiological origin. In a 2006 survey from the UK, 21.4% of 3,707 small animal consultations were for flea infestation/allergy dermatological problems making it the second most common diagnosis in cats and the fourth most common diagnosis in dogs.

With respect to the pathogenic effect of flea infestation, a differentiation must be made between the allergic reaction of the host and the effect of blood consumption by the parasite. Flea bite hypersensitivity, also known as flea allergy dermatitis (FAD), is a disease in which a state of hypersensitivity against antigenic material from fleas is induced in a host. This occurs mainly in response to the injection of such material from the fleas’ salivary glands. Type I hypersensitivity reactions are of central importance in the development of clinical signs. And sustained clinical improvement of FAD can only be achieved by preventing the sensitized animal from

<table>
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<tr>
<th>Family</th>
<th>Pulicidae</th>
<th>Ceratophyllidae</th>
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<tr>
<td>Genus (e.g.)</td>
<td>Archaeopsylla, <em>Ctenocephalides</em>, <em>Echidnophaga</em>, <em>Pulex</em>, <em>Spilopsyllus</em>, <em>Xenopsylla</em></td>
<td>Ceratophyllus, Nosopsyllus</td>
</tr>
<tr>
<td>Species (e.g.)</td>
<td>A. <em>erinacei</em> (hedgehog flea)&lt;sup&gt;b&lt;/sup&gt; \ C. <em>canis</em> (dog flea)&lt;sup&gt;b&lt;/sup&gt; \ C. <em>felis</em> (cat flea)&lt;sup&gt;a,b&lt;/sup&gt; \ E. <em>gallinacea</em> (sticktight flea)&lt;sup&gt;a&lt;/sup&gt; \ P. <em>irritans</em> (human flea)&lt;sup&gt;a,b&lt;/sup&gt; \ S. <em>cuniculi</em> (rabbit flea) \ X. <em>cheopsis</em> (oriental rat flea)</td>
<td><em>Ce. gallinae</em> (common hen flea)&lt;sup&gt;a&lt;/sup&gt;</td>
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Tab. 1 Taxonomy of fleas (see references 59 and 60).

a) Of importance in dogs and cats in the USA; b) Of importance in dogs and cats in Europe and other parts of the world.
being bitten by fleas. To differentiate FAD from other similar diseases, useful diagnostic tests are presented in Table 2.

The clinical signs in dogs and cats are the result of pruritus and self trauma and depend on the frequency of flea exposure, the duration of the disease, the presence of secondary or other concurrent skin disease, the degree of hypersensitivity, and the effects of previous or current treatment (see Figure 3). The extent of dermal lesions can vary from relatively few spots to large areas depending on the factors listed above.

Besides dermal changes, blood feeding of adult fleas can cause quite substantial blood loss in very young animals. Seventy-two female fleas can consume up to 1 ml of blood daily. Thus, an infestation of 220 female fleas could potentially consume 10.0% (i.e., 3.0 ml) of a 0.45-kg kitten’s blood per day. In mature cats, dogs, or young livestock with comparatively greater blood volume and iron reserves, very high infestation levels would need to be maintained over several weeks to produce chronic blood loss and anemia.

Humans are particularly affected when large numbers of fleas suddenly and synchronously hatch from their waiting stage. This can happen on return or moving to habitations which had previously been abandoned by infested pets and their owners for a certain length of time. The direct effects of flea bites in humans usually present as strongly pruritic papules and plaques, often arranged linearly or in groups, with a central hemorrhage (see Figure 4). In children with an increased immunological reaction, large bacterial plaques, blistering, or multiple infections have been quite frequently recorded.

Transmitted canine pathogens with public health background

For the last few years, an increasing number of reports have been dealing with so-called canine-vector borne diseases (CVBD), like babesiosis, leishmaniosis, ehrlichiosis, or heartworm disease. There are major concerns about the introduction of pathogens into former non-endemic areas as well as new insights into diseases with emergent pathogens, like *Dirofilaria repens* or rickettsial bacteria. Besides ticks, mosquitoes, and sand flies, which are capable of transmitting the vast majority of canine pathogens,
fleas should also be considered. A selection of mainly canine pathogens, which additionally possess public health implications, is given below (see also Table 3).

**Bartonella spp. transmission**

During the last 10 to 15 years, infections with *Bartonella* spp. have been reported with increasing frequency (see Figure 5), a trend which also includes the dog as a potential patient.

Besides cats, which play an important role as a confirmed reservoir of the cat scratch disease (CSD) pathogen *Bartonella henselae*, dogs have also been reported to be infected with different *Bartonella* species (*B. vinsonii* ssp. *berghoffii*, *B. henselae*, *B. clarridgeiae*, *B. washoensis*, *B. elizabethae*, and *B. quintana*). Four *Bartonella* species have been detected in dog saliva.

Dogs may, often in contrast to cats, develop clinical signs that are similar to those observed in humans. All of the above-mentioned pathogens in dogs have been associated with variable pathology and clinical signs in the canine host, including endocarditis, cardiac arrhythmias, myocarditis, granulomatous rhinitis, anterior uveitis, choroiditis, hepatic disease, and sudden death. *B. henselae* furthermore has been implicated in peliosis hepatis, granulomatous hepatitis, and granulomatous sialadenitis. *B. henselae* and *B. quintana* have also been detected in the blood or lymph nodes of dogs suffering from lymphoma. *B. henselae, B. clarridgeiae, B. quintana,* and *B. koehlerae* have also been reported to be transmitted mainly by cat fleas (see also Table 3) or by cat fleas in addition to other ectoparasites like lice and ticks.

From a public health perspective, bartonellosis is with increasing frequency considered an emerging zoonosis. *B. henselae* and *B. clarridgeiae* are two agents of CSD, possessing clinical importance in man. However, direct transmission is questionable and has so far been reported mainly in association with scratches from infected animals (primarily cats, but also reported from a dog). *B. quintana*, the agent of ‘Trench fever’, causes endocarditis and bacillary angiomatosis in man. *B. koehlerae* may also cause endocarditis. Recently, *B. henselae* and *B. vinsonii* ssp. *berghoffii* were detected in the peripheral blood of immunocompetent patients suffering from chronic neurological symptoms including ataxia, seizures, and tremor.

Of all listed *Bartonella* species, *B. henselae* is the most important representative as the main causative agent of CSD. In regard to the vector capacity of fleas and considering that the dog is also suggested to represent a reservoir for this pathogen besides cats, the possibility of *B. henselae* transmission from dogs to humans should not be ruled out. Published examples include osteomyelitis in a human after a dog scratch and lymphadenopathy in a dog owner (seroreactive for *B. henselae*).

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**Fig. 4** Human leg showing flea bites and flea-associated dermatitis.

**Table 3**

<table>
<thead>
<tr>
<th>Category</th>
<th>Pathogen</th>
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<tr>
<td><strong>Helminths</strong></td>
<td><em>Dipylidium caninum</em> (dog tapeworm)</td>
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<td></td>
<td><em>Hymenolepis nana</em></td>
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<td></td>
<td><em>H. diminuta</em></td>
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<td></td>
<td><em>H. citteri</em></td>
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<td></td>
<td><em>H. microstoma</em></td>
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<td></td>
<td><em>Dipetalonema reconditum</em></td>
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<tr>
<td><strong>Bacteria</strong></td>
<td><em>Rickettsia typhi</em></td>
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<td></td>
<td><em>Rickettsia sp.</em></td>
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<td></td>
<td><em>R. felis</em> (former ELB-agent)</td>
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<tr>
<td></td>
<td><em>Bartonella henselae</em></td>
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<tr>
<td></td>
<td><em>B. clarridgeiae</em></td>
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<tr>
<td></td>
<td><em>B. quintana</em> (mainly body louse as vector)</td>
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<tr>
<td></td>
<td><em>B. koehlerae</em></td>
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<td></td>
<td><em>Yersinia pestis</em></td>
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<td></td>
<td><em>Pasteurella</em> sp.</td>
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<tr>
<td></td>
<td><em>Brucella melitensis</em></td>
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<td></td>
<td><em>Br. abortus</em></td>
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<td></td>
<td><em>Br. suis</em></td>
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<td><strong>Viruses</strong></td>
<td><em>Feline calicivirus (FCV)</em></td>
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<td></td>
<td>Friend Leukemia Virus <em>Cheyletiella parasitivorax</em></td>
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<tr>
<td></td>
<td><em>Cheyletiella sp.</em></td>
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(Literature can be obtained from the author).
DNA had been amplified from gingival swabs of the dog. It has been assumed that vector control (flea and tick) reduces the risk of transmission from fleas to dogs and, thus, possibly from dogs to humans.

Plague transmission
Plague, the most devastating infection in the history of mankind, was always believed to be transmitted by the rat flea, *Xenopsylla cheopsis*, if transmitted by ectoparasitic vectors at all. Cat fleas were not regarded as competent vectors of the plague bacteria. In cases where pets infect their owners, direct pneumonic transfer or bites from infected rodent fleas residing temporarily on their pets have been considered responsible. More recently, dogs have been shown to be capable of carrying the etiologic agent of bubonic plague, *Yersinia pestis*. In a study in Tanzania, 5.5% of 201 healthy dogs in plague-infected villages showed significantly elevated plague-specific antibodies. Those dogs were also heavily infested with fleas and, typically for dogs, cat and dog fleas were detected (93.8% *C. felis* and 6.2% *C. canis*). In addition, *C. felis* has also recently been reported as a competent vector of plague bacteria, but with low efficiency compared to other flea species. Nevertheless, it could play a significant role as secondary vector and should not be ignored in plague control programs.

Helminth transmission
Fleas are the intermediate host of the universally distributed cestode *Dipylidium caninum*. Infection of the dog follows ingestion of infested fleas. The prevalence in the flea population has been recorded with every 44th flea from cats and 61st flea from dogs, bartonellosis is considered to be a canine vector-borne disease (CVBD).

INFO BOX 1

**BARTONELLA**

Bartonellae are gram-negative bacteria causing various human and canine diseases. They can be transmitted by various arthropod vectors as well as through direct transmission via bites and scratches. Because of transmission via fleas and presumably also ticks in cats and dogs, bartonellosis is considered to be a canine vector-borne disease (CVBD).

Rickettsia felis infection
The former ELB-agent *Rickettsia felis* has been reported as an emergent rickettsial pathogen with a worldwide distribution in mammals, humans, and ectoparasites. The clinical manifestations of *R. felis* infection in humans resemble those of murine typhus and dengue, and so far it is questionable whether *R. felis* requires only fleas for its maintenance in nature. Cat fleas collected from dogs have been shown to be positive for *R. felis*, but clinical symptoms have not been reported in any animal carrying positive fleas so far. The current knowledge suggests that the only role of mammals/dogs infected with *R. felis* is probably to amplify the cycle of
fleas feeding on their R. felis-infected blood, which nevertheless brings man into potential contact with this pathogen via his best companion, the dog.

**Issues of reduced susceptibility**

The major cause of failure to eradicate fleas on a pet is a combination of insufficient control and client education, while the issue of resistance is often blamed. For a long time, there has been an ongoing discussion on the potential resistance of fleas to insecticides. Cat fleas have been shown to be resistant to a number of active ingredients (e.g., chlordane, dieldrin, and hexachlorocyclohexane (HCH)). However, documentation and evidence of resistance is complicated by susceptibility variation, bioassay conditions, and strain differences in C. felis. To overcome part of these problems and to closely monitor the susceptibility against one of the well-known flea ectoparasiticides, the "Imidacloprid Flea Susceptibility Monitoring Team" was founded in 1999 and has been testing flea isolates from all over the world since that time. This monitoring initiative supported by Bayer Animal Health was formed to observe imidacloprid susceptibility among cat fleas collected from the field on a global basis. A larval bioassay was established and a diagnostic dose (DD) of 3 ppm imidacloprid in larval rearing media was fixed to detect shifts in tolerance as a possible consequence of incipient reduced susceptibility to imidacloprid. Examination of 768 flea isolates revealed 6 isolates in the bioassay with a survival rate greater than 5%. However, in further evaluations of their susceptibility to imidacloprid, these isolates did not finally differ from the reference strains. Ongoing collections will continue in an attempt to detect and document any change in the susceptibility of field flea collections to imidacloprid, to the benefit of the consumer.

**Flea control to achieve reduction of disease transmission in pets**

When it comes to flea control, it is very important for the pet owner to understand that animals and the environment must be treated at the same time and that continued treatment at regular intervals will be necessary. For a successful management of FAD in pets and potential disease transmission to other domestic animals and humans, a three-pronged flea control program is advisable, consisting of:
- treatment of the pet
- treatment of all contact animals
- potential treatment of the environment (indoors and outdoors)

The control program should be individualized based on the number of animals in the environment, the size of the indoor environment, the degree of outdoor exposure to fleas, the size of the outdoor area, the time of year, and the family situation, such as the presence of young children. Treatment of the premises can be achieved by insecticide application, but also by thorough sanitation. This includes repeated vacuuming of carpets, furniture, floors, and baseboards, possibly steam-cleaning of the carpeting, washing or deep-freezing of frequently used sleeping areas. Flea control and reduction of flea infestation on the pet can be achieved and maintained by a regular use of on-animal applied insecticides. A vast number of active ingredients are available for flea control on the pet as well as in the environment. In a comparative study with four topical active ingredients against adult fleas, imidacloprid has been shown to provide a significantly greater flea kill at diverse time points. A single application provided a high efficacy in the early elimination of adult fleas suggesting a high speed of kill for imidacloprid.

The success of the flea control program will also be determined by choosing a delivery system that is efficient and fits the animal's personality as well as the owner's schedule. The use of a flea comb is advisable if a pet is too young or too sick to be treated with insecticidal preparations. Depending on the clinical presentation, allergic reactions should be controlled by supportive medical therapy such as systemic glucocorticoids and possibly antibiotics in case of secondary pyoderma. The best prevention of flea-transmitted diseases is achieved by avoiding or minimizing the exposure to the vector, as with other CVBD that are transmitted by ticks, mosquitoes, and sand flies. In the case of fleas this is nearly impossible in free-roaming animals. Consequently, regular application of highly efficient ectoparasiticides is advisable. In addition, using a broad-spectrum ectoparasiticide with repellent properties would help to control other vector-borne diseases transmitted by vectors apart from fleas.
References
