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It shouldn't happen to a dog … or a veterinarian: clinical paradigms for canine vector-borne diseases

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Abstract

Canine vector-borne diseases (CVBDs) comprise a diverse group of viral, bacterial, protozoal, and helminth pathogens, transmitted predominantly by ticks and fleas, and cause significant health problems for dogs worldwide. Growing numbers of reports indicate that CVBDs are emerging in regions where they previously did not exist and this, combined with pathogens that are inherently difficult to detect, is providing companion animal veterinarians with some significant diagnostic challenges. This review discusses six paradigms concerning the diagnosis, treatment, prevention, and zoonotic implications of CVBDs from a veterinary clinical perspective.

Dogs, veterinarians, and canine vector-borne diseases

Globally, pet ownership is increasing, with an estimated 63% of US households having at least one pet. In 2010, dogs accounted for the majority of family pets in Australia (3.41 million), and in the European Union it was estimated that 27% of 70 million households own at least one dog [1,2]. In the UK there are approximately 8 million dogs [1]. In addition to family pets, dogs are used extensively in farming, for people with disabilities, with the military (often serving in regions where the risk of vector-borne disease is greater than in their home countries), and in many other facets of community life. Although data regarding dog populations in the developing world are incomplete, ownership of dogs as family pets (as distinct from roaming and feral populations) is growing in popularity, and with this comes increased provision of veterinary care [3]. Importantly, such countries are mostly situated in tropical regions of the world, where the climate favours ectoparasite life cycles and facilitates the transmission of vector-borne diseases. While numerous health and social benefits arising from the human-companion animal bond are beyond question, zoonotic diseases associated with companion animal ownership are increasingly receiving the attention of healthcare professionals, policy makers, and the general public [4].

Veterinarians are the key professionals at the companion animal: human interface. Not only do they provide the traditional medical and surgical services for pets, their training in the disciplines of parasitology, microbiology, epidemiology, and public health place them in a unique position to provide advice about matters pertaining to vector-borne diseases. Despite this, emerging canine vector-borne diseases (CVBDs) pose a number of significant and complex challenges for veterinarians in clinical practice whose responsibility it is to diagnose and treat these companion animals, while at the same time remaining mindful of the potential for disease transmission to the owners and other people living in close proximity, as well as to other susceptible animals [5]. As will be discussed here, many CVBDs are caused by organisms that are inherently difficult to detect, frequently cause nebulous clinical signs in their canine hosts, and are sometimes zoonotic. In addition, the rapid progress of scientific research in this area itself poses further challenges of how best to distil and disseminate this knowledge to busy veterinary practitioners worldwide at a time when every aspect of clinical practice is becoming more complex. How should practitioners keep current with information in this area so that they can provide appropriate evidence-based advice to their clients?

Ectoparasites and the canine vector-borne diseases

Vector-borne diseases are caused by viruses, bacteria, protozoa, and parasitic helminths, transmitted during feeding activities of haematophagous (see Glossary) arthropods or, in some instances, when the arthropod itself is ingested. Ticks, fleas, and sand flies are vectors of the most significant CVBDs (Table 1). Information about the aetiological and clinicopathological characteristics of these diseases, together with therapeutic considerations, are traditionally taught within veterinary microbiology and parasitology courses of the veterinary degree programs and reinforced, at least for locally prevalent diseases, during clinical rotations and internships in the latter years of veterinary training at most universities. For reasons that will become apparent here, it is critical that these remain firmly embedded as core disciplines within the veterinary curriculum and do not become marginalised by a focus on clinical training within mainstream veterinary education [6]. Veterinarians require a sound foundation in pre-clinical sciences together with robust clinical problem-solving skills to meet the challenges posed by emerging infectious diseases, new data about zoonotic pathogens, and looming resistance to commonly used parasiticides.

Clinical paradigms

In an expression of concern about the growing threat posed by the rapid spread of CVBDs and in recognition of the pivotal role played by veterinarians in managing the impact of these diseases, a group of veterinarians, parasitologists and infectious disease experts of the CVBD World Forum (www.cvbd.com) developed a series of recommendations for veterinarians for the diagnosis and management of CVBDs (Box 1) [7]. These recommendations are further explored and adapted here into a series of clinical paradigms.

Paradigm 1: forget about 'exotic' disease – expect the unexpected

The adage 'common things are common' is sometimes used to describe the incidence of certain diseases in medicine (and by extension, in veterinary science) but this serves only to remind us that sometimes a rare diagnosis is the right one. Veterinarians need to be aware that a pet dog could present at any time with an infection or disease that they last heard about in veterinary school. Increasingly, unexpected canine infectious and parasitic diseases are reported in localities where they have never before been recognised [8-10], and the epithet 'exotic disease' appears to be in danger of becoming redundant. As an example, the term 'oriental eye worm' for *Thelazia callipaeda* (a vector-borne nematode of domesticated and wild canids) refers to its originally recognised distribution in Asia and the 'Far East' (from a Eurocentric perspective). However, this zoonotic parasite is rapidly emerging as a disease problem in animals and people in Mediterranean countries, and recent cases in Belgium, Germany, and Switzerland [11-13] have confirmed predictions inferred by ecological modelling [14] that its insect vector, *Phortica variegata,* might establish across much of Western Europe.

Some cases of emergent CVBDs can be explained relatively easily when travel history is collected. In Europe, good roads and the Schengen Agreement have facilitated travel, and driving holidays with the family dog(s) are popular. In a study of dogs diagnosed with *Babesia canis* or *Ehrlichia canis* in The Netherlands, most (84%) had visited an endemic area such as the Mediterranean or the Dutch Antilles (in the Caribbean) previously [15]. Vacation-associated pet travel is not the only way that CVBDs can be disseminated; in a salutary lesson on the spread of infectious diseases, many dogs rescued in the wake of the Hurricane Katrina disaster were re-homed throughout North America, resulting in wide dispersal of infectious diseases of animal and zoonotic importance throughout the continent [16]. Additionally, despite the high level of veterinary care they receive, military working dogs in various theatres of operation around the world are at great risk of contracting vector-borne disease [17]. Imported CVBDs have been described with increasing frequency in recent years not only in Europe [18] but in other parts of the world including Japan [19] and Australia [20]. These examples not only emphasise the importance of obtaining travel history of the dog during every veterinary consultation, but of developing a general awareness of a client's travel schedules.

Some instances of autochthonous CVBDs arise from direct contact between dogs (or in rare cases, just with the owners) that travelled from endemic regions [21], rather than via a vector. In such cases information pertaining to travel may not be apparent, and contact with the infected dog may be overlooked. For example, it is common practice for dogs of prized blood lines to travel interstate or overseas for stud purposes, and pups born to bitches infected with *Leishmania* spp. at a distant location have been reported to develop canine leishmaniosis as a result of either transplacental transmission of the parasite or direct dog-to-dog contact (when insect vectors are considered unlikely) [22-23]. Canine babesiosis, specifically *Babesia gibsoni*, is transmitted horizontally, without a vector, when there is fresh blood exchanged between dogs during fighting [24], and in such cases there may be no immediate history of travel in any of the affected individuals. In this example, the signalment of the dog (particularly its breed) should provide the veterinarian with useful diagnostic clues (providing they are aware of this association), but non-fighting breeds may also become infected with *B. gibsoni* [25]; and in such situations a misdiagnosis of immune-mediated disease (haemolytic anaemia or thrombocytopenia) might be made.

Cases of autochthonous disease that arise without warning in localities far from previously recognised endemic regions are of particular concern for veterinarians and pet owners. Here, the all-important clinical suspicion normally triggered by reference to travel history is missing. Severe and sometimes fatal clinical illness associated with canine babesiosis, monocytic ehrlichiosis, and leishmaniosis were described recently in untravelled dogs in Europe; in the UK [26-27], Norway [28] and Hungary [9]. Depending on the circumstances, such cases may go undiagnosed (more generally misdiagnosed) during which time there may be opportunities for non-vectored transmission of the disease to occur to other dogs as described above. Practicing veterinarians need to know whether these cases represent isolated, and seemingly improbable, misfortune (a naive dog is bitten by a recently introduced infected tick) or if they represent the establishment of new vector-pathogen-host ecologies in their local area [29]. Despite autochthonous cases of canine babesiosis reported in Belgium in recent years, no evidence of *Babesia* DNA was detected in field-collected ticks in one study [30]. However, the application of new gene sequencing technologies is starting to facilitate the study of microbial communities within haematophagous arthropods using a deep sequencing approach. Techniques such as ion semiconductor and 454 pyrosequencing should not only enhance our understanding of the taxonomic diversity of enzootic pathogens, they may also inform risk assessments for vector-borne diseases in both humans and companion animals [31].

In some situations it is the invertebrate vector, rather than the infected mammalian host, that is introduced to a new location, accompanied by its potentially pathogenic microorganisms. The vector may travel on the host or may be contained within inanimate objects such as furniture or clothing. The brown dog tick (*Rhipicephalus sanguineus* sensu lato) (Figure 1A and B) is able to establish in protected habitats in temperate climates (e.g., indoors, especially when there is central heating), far from its usual tropical and subtropical habitats [32-34]. Interestingly, recent research confirms that ticks identified as *R. sanguineus* actually represent a group of species [35] and this new information may help to explain sometimes incongruent data about the biology, ecology and vector competence for certain pathogens attributed in the past to the brown dog tick [35]. The ability of a vector arthropod to establish in a new locality is not solely dependent on an appropriate microclimate, although climate change is hypothesised as facilitating the process, but requires suitable vertebrate host species to maintain its life cycle stages, and potentially amplify the pathogenic microorganism. For ticks to be a competent vector, more than one instar must acquire a blood meal from a given host species. The parameters required for successful transmission of vector-borne diseases are complex and relate, among other things, to the number of vectors in contact with a given individual, the number of vector bites/day on individuals, the survival rate of the vector, the duration of the pathogen's development cycle in the vector, vector competence, the infectivity of the infectious agent, and the host's infectiousness clearance rate [36-37].

Pet ownership practices around the world have changed to such an extent that a dog harbouring a vector-borne infection, clinically or sub-clinically, may be presented to a veterinarian at any time. Rather than selecting the diagnostic hypothesis with the fewest assumptions, referred to as Occam's razor, veterinarians working on the frontline of clinical practice should embrace a new paradigm: to expect the unexpected and endeavour to incorporate a greater awareness of CVBDs into their diagnostic protocols.

Paradigm 2: maintain the (clinical) vigilance

Being able to diagnose the cause of illness is a fundamental skill for veterinarians, who are trained in diagnostic reasoning through a process that combines an understanding of pathophysiology and manifestations of disease with historical and clinical data gathered during the consultation process and physical examination of the patient [38-39]. Yet, within the myriad of disease conditions encountered every day in clinical practice how can a veterinarian be expected to maintain an appropriate level of watchfulness for CVBDs?

Increasingly, problem-orientated medical diagnosis (POMD) has been adopted by veterinarians as a logical and systematic approach to clinical diagnosis. Clinicopathological abnormalities (diagnostic 'problems') consistent with infectious disease aetiology are listed in Table 2, but many of these are shared with immune-mediated, neoplastic, and other systemic causes of disease. However, there is a growing realisation that certain disorders in dogs which have frustrated veterinarians for many years, previously designated 'immune-mediated' (e.g. immune-mediated haemolytic anaemia), or 'idiopathic', may actually result from persistent infection with one or more so-called 'stealth pathogens'. Indeed, the complexity of proving disease causation by organisms such as *Bartonella* has recently prompted the proposal that a fifth postulate should be added to Koch's postulates [40].

One of the most helpful advances in the diagnosis of CVBDs in recent years has been the development of in-house, rapid immunochromatographic tests that detect antibodies (or antigens) associated with infection by the most widespread CVBDs (e.g., ehrlichiosis, anaplasmosis, leishmaniosis, borreliosis, and dirofilariasis) (Table 1). These are not only more convenient and generally cheaper than traditional serological techniques (e.g., immunofluorescent antibody testing), they have the important advantage in the clinical setting of empowering the veterinarian to provide immediate treatment for the pet and advice to the owner. An additional benefit of these tests, often with in-kind support provided by the manufacturers, has been an increase in the number of cross-sectional serosurveys of CVBDs around the world, which have greatly furthered our understanding of their epidemiology and geographical distribution [41,42]. Nevertheless, it should be remembered that such tests also have limitations in terms of sensitivity (e.g., acute infections prior to antibody response) and specificity (e.g., cross-reactions between organisms), and some clinically significant diseases (e.g., acute babesiosis) are still probably best diagnosed by microscopy [43,44].

Unfortunately, not only is the clinical suspicion for vector-borne disease often low, or missing altogether for reasons described previously, many CVBD pathogens are also inherently difficult to detect. There are several reasons for this; the clinical signs associated with vector-borne diseases in dogs are frequently non-specific, and co-infections – another hallmark of CVBDs – may alter the clinical picture typically associated with a single pathogen [45,46]. Some dogs remain carriers for long periods of time, only developing clinical signs either late in the course of infection (e.g., leishmaniosis) or when the dog becomes immunocompromised as a result of another disease process such as cancer. In addition, although the presence of ticks, fleas, or any other ectoparasite on the patient would prompt a veterinarian to investigate potential CVBDs, seasonal factors and periodic application of ectoparasiticides by the owner mean that arthropods are not always observed during routine veterinary examinations. Maintenance of a clinical vigilance for CVBDs should prompt the veterinarian to check an owner's compliance with ectoparasiticide prophylaxis.

While the development of in-house diagnostic kits has been a welcome addition to the diagnostic armoury, these are generally available for only the most common CVBDs, and a significant diagnostic challenge remains for pathogens that are less commonly associated with dogs, yet are frequently zoonotic (Table 3). Not only is detection of these organisms currently restricted to relatively few research laboratories worldwide, stealth organisms also require advanced diagnostic methodologies and complex protocols for successful identification [47]. The sensitivity of detection of *Bartonella*, for example, is improved considerably by pre-PCR microbial culture in enrichment medium [48,49]. Such restrictions add complexity to the diagnosis for veterinarians in countries with access to good laboratory support, but these protocols and costs are usually well beyond the means of owners to pay for them in developing countries where the need is arguably higher, and where much remains to be discovered about CVBDs [50]. Finally, since multiple co-infections frequently occur, the diagnosis of one CVBD should immediately raise the clinical suspicion for the presence of other vector-borne pathogens in the dog, and appropriate diagnostic testing should be scheduled.

Paradigm 3: fleas are more than simply a nuisance

Although ticks were the first arthropods to be recognised as vectors of disease in animals and remain, in terms of the diversity of the canine pathogens they transmit, the quintessential group of ectoparasite vectors in dogs [51,52], it is probably fair to say that most dog owners would more readily identify fleas (or flea infestation) as one of the pet health issues of greatest concern. It is expected that veterinarians would also identify the dermatological disease caused by fleas as among the most common problems in companion animal practice; it is estimated that fleas are a factor in > 50% of small animal dermatology cases. However, in addition to being annoying, fleas are effective vectors of disease, and new research into bartonellosis and flea-borne rickettsiosis in particular, is starting to inform us just how important fleas are in terms of CVBDs and zoonotic infections [53]. Fleas are much more significant from a health perspective than previously assumed; veterinarians need to educate their clients about minimizing transmission risk and play a vital role in the prevention of flea-borne zoonotic disease.

Certain flea-borne zoonoses that have caused disease epidemics in the past, such as plague and murine typhus, are not usually associated with dogs, yet one recent study into dog-associated risk factors for human plague revealed that within case households with multiple family members, sleeping in the same bed as a pet dog was significantly associated with infection with *Yersinia pestis* [54]. This finding is relevant for other dog-associated, flea-borne pathogens such as *Rickettsia felis*, the cause of flea-borne spotted fever. Despite its name, recent data [55] suggest it is dogs, not cats, that are the peri-domestic mammal reservoir for *R. felis*; perhaps this should not come as a surprise since *R. felis* has proved elusive to isolate from cats [56,57], yet the cat flea (*Ctenocephalides felis*) – widely recognised as the vector for *R. felis* – parasitises dogs with alacrity (Figure 2). Nevertheless, ectoparasiticides should be applied to both dogs and cats to prevent the spread of this disease.

Cat scratch disease (CSD) in humans is typically caused by *Bartonella henselae*, a Gram-negative bacterium that is highly adapted to domestic cats and wild felids, establishing persistent, usually asymptomatic (stealth) infections in these vertebrate hosts. Importantly, however, many people who contract *Bartonella* infections report never having been bitten or scratched by cats [58], and arthropod (flea)-borne transmission is recognised as the most likely mode for the development of infection in these circumstances. In the last ten years a picture of enormous complexity with significant potential implications for public health has emerged with regard to the species diversity and clinical manifestations of *Bartonella* spp. infections (bartonellosis) in humans and animals. Rather than being confined to CSD, it is apparent that human and canine bartonellosis encompass pathological syndromes of vasoproliferative pathology, granulomatous inflammation, and endocarditis [59] associated with long incubation times, persistent infections, and arthropod transmission [59]. Animal contact, and therefore contact with their ectoparasites, puts certain individuals at risk of contracting *Bartonella*-associated disease, which may remain undiagnosed for many years [59,60].

Paradigm 4: CVBD, veterinarians and public health

Recognition that human health, animal health and the health of the environment are inextricably linked is at the core of the One Health initiative. Through their occupation, veterinary professionals (veterinary surgeons, veterinary nurses, and technicians) and animal carers (animal welfare workers, rangers, shelter staff, etc.) are in contact with a wide range of companion, production, and wild animal species and, by extension, are frequently exposed to arthropod vectors such as ticks, fleas, and lice that infest these animals (Figure 3) [60]. Despite this, and the potential for contracting zoonotic infections, about half of the veterinarians questioned at a national veterinary conference perceived that they were at low level of risk of being exposed to zoonotic diseases from various animal species and procedures [61]. The reasons for this perception are not clear but maybe reflect a certain complacency that the species 'barrier' may protect them whilst working with pets. Indeed, the same study found that small animal practitioners were three times less likely than their large animal colleagues to use adequate personal protective equipment (PPE) [61]. In the

USA, *Bartonella* seroreactivity and bacteraemia were documented in approximately one half (49.5%) and a quarter (23.9%) of the individuals, respectively, of persons (n=192) who reported animal exposure, most of whom also reported animal scratches and/or bites [60]. While certain zoonoses (e.g., canine rabies), are very well known, the risks associated with vector-borne diseases may be less well appreciated, and some that are currently considered not to infect humans may turn out to be pathogenic in the future. For example, co-infection of a female veterinarian by *Bartonella henselae*, *Anaplasma platys*, and *Candidatus* Mycoplasma haematoparvum was reported recently and, importantly in this context, the latter two organisms were known previously to only infect dogs [62]. The emergence of infectious viral hepatitis and HIV resulted in the universal adoption of comprehensive protective practices within the human medical community [63]; maybe this case should serve as a reminder that there is much to understand about risks to veterinarians, and this paradigm calls for a cultural change in work practices and attitudes in regard to vector-borne infections [61].

Studies involving dogs and other animals can complement epidemiological research into zoonotic vector-borne diseases, and by sampling companion animals veterinarians are able to contribute data to assist in the surveillance of diseases of public health importance. Dogs are readily infected by ticks as a result of their close proximity to the ground and their behaviour of exploring in the undergrowth. Pet dogs may therefore contribute information about the infection risk for people in a given area, either through serological test results that indicate exposure to vector-borne zoonotic pathogens [64-66], or as 'tick magnets' that reflect the local pathogen-vector ecologies when subjected to molecular screening [29,67]. Dogs are known to be sentinels for Lyme borreliosis, anaplasmosis and ehrlichiosis in people [66,68, 69], and it has been suggested they might also serve as sentinels for tick-borne encephalitis and Japanese encephalitis virus in Europe [70]. The value of using dogs to unearth new information was highlighted during a nationwide serological survey of vector-borne pathogens in the USA during which two unexpected foci of *E. canis* reactivity were detected in dogs in Wisconsin and Minnesota [71]. *E. canis* is transmitted by the brown dog tick and its close relative *Ehrlichia chaffeensis* (that also reacts serologically in the same test) is transmitted by *Amblyomma americanum*; yet neither tick species is enzootic in these regions. Subsequent studies, however, revealed the presence of a novel ehrlichial pathogen of people [72], and it was presumed that exposure of dogs living in these areas to *Ixodes* ticks, considered the most likely vector, resulted in immunological cross-reactivity in the *E. canis* test. Interestingly, since these studies were reported, at least one case of clinical illness associated with *Ehrlichia muris* infection has been documented in a dog living in Minnesota – returning us once again to the first paradigm discussed in this review, to expect the unexpected [73].

Although healthy pets unquestionably bring their owners many benefits, ranging from improved mental health to physical well-being, it is inevitable that questions are raised from time to time about whether pets may place their owners at increased risk of zoonotic infections. With regard to vector-borne zoonoses it is conceivable that the close association owners have with dogs may place them at increased risk of environmental exposure to pathogen-laden ticks, fleas, or other arthropod vectors. On the one hand, leisure activities in rural areas such as walking a dog [70] are risk factors for acquiring vector-borne diseases, primarily because of increased exposure to questing ticks of all stages. On the other hand, arthropod vectors brought into or attracted to the home by dogs may inadvertently bite humans sharing this space. The presence of companion animals within the home environment is a definitive risk factor for human infection with *Trypanosoma cruzi* and leishmaniosis, for example [74,75]. Veterinarians clearly have an important role in educating their clients about minimizing transmission risk.

Paradigm 5: prevention is better than cure

In the light of the foregoing, it is apparent that protection from ectoparasites has never been so important, not only to prevent disease in the dogs themselves, but to reduce also the risk of zoonotic disease. It is ironic, therefore, given the complexities and potential seriousness of CVBDs, that their prevention is relatively simple. Apart from infrequent cases of direct dog-to-dog (non-vectorial) transmission discussed previously, stopping ectoparasites from feeding on a host will prevent the transmission of vector-borne disease. Here once again the veterinarian's advice is critical for the education of dog owners about the choice of appropriate ectoparasiticides. Fortunately, the choice of ectoparasiticides available for companion animals has improved in recent years. The days of 'flea powder' as the mainstay of ectoparasite control are long past, and dog owners have a wide variety of insecticidal and acaricidal sprays, 'spot-ons', dips, rinses and shampoos, orally administered tablets, and chemically-impregnated collars to choose from. Such products contain not only pulicides and acaricides, some also contain insect growth regulators (IGRs), or insect development inhibitors (IDIs) that exert their action by interfering with the development of the eggs or other off-host life-cycle stages, and some have repellent agents (e.g., permethrin) that discourage arthropods from attaching to the host [76].

A veterinarian's contribution extends beyond prescription of an appropriate ectoparasiticide; they also play a vital role in ensuring that owners understand how to use the product. Failure to apply an ectoparasiticide correctly jeopardises the entire strategy [77]. Breakdown in ectoparasite control programs are thought to occur frequently, and poor owner compliance is an important reason for this [78]. Use of the incorrect frequency of application or dose of the product through misunderstanding or oversight is common, risking ectoparasite attachment, feeding and pathogen transmission [78]. Application of the product by the wrong route, such as inadvertent oral administration of a spot-on product has been recorded [79]. All staff in a veterinary practice that meet clients should be familiar with the principles of ectoparasiticide usage and encourage pet owners to engage in the process.

Paradigm 6: continuing education is critical

Remaining current in terms of discipline-specific knowledge is a challenge for many professions in the face of rapidly expanding information. Excellent resources are available including articles in scientific journals, on-line webinars (e.g., see www.cvbd.org) and seminars presented by pharmaceutical companies, and internet resources provided by organisations such as the Companion Animal Parasite Council (www.capcvet.org) and its European equivalent (www.esccap.org). Together, these resources educate and inform veterinarians not only about new pharmaceutical products, but also about scientific advances and ever growing information about parasites and their vectors.

Concluding remarks

Rapid growth in recent information about CVBDs seems to be outstripping our ability to disseminate it effectively to the veterinary profession, thereby increasing the risk that these pathogens will continue to spread through the world's canine population. Veterinarians should take the time whenever possible to update their knowledge about these scientific breakthroughs in order to improve their diagnostic proficiency and to safeguard the health of their patients, their patients' owners, their staff, and of themselves.

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Glossary

Acaricide: An agent that kills members of the order Acarina, specifically ticks and mites.

Autochthonous: Originating in the same area in which it is found.

Clinicopathological: Pertaining to both signs of disease and to its pathology.

Companion Animal Parasite Council (CAPC): An independent council established to create guidelines for the optimal control of internal and external parasites that threaten the health of pets and people, brings together broad expertise in parasitology, internal medicine, public health, veterinary law, private practice, and association leadership.

CVBD World Forum: A multidisciplinary group of experts in CVBD from around the world which meets on an annual basis. The CVBD World Forum is supported by Bayer Animal Health.

Enzootic: Occurs endemically (i.e., constantly in a location) among animals.

European Scientific Counsel Companion Animal Parasites (ESCCAP): An independent, non-profit making organization consisting of experts in the field of parasitology and public health from across Europe.

Haemolytic anaemia: Anaemia caused by increased destruction of erythrocytes.

Haematophagous: Blood feeding.

Idiopathic: Occurring without known cause.

Insect development inhibitor/ Insect growth regulator: An agent that exerts its action by interfering with the development of the egg or other off-host life-cycle stages of insect ectoparasites.

Koch's postulates: A statement, originally made by German bacteriologist Robert Koch, about the kind of experimental evidence required to establish the causative relation of a given microorganism to a given disease. Four postulates are currently widely accepted.

Neoplastic disease: Disease associated with a tumour.

Peri-domestic mammal reservoir: Mammals (e.g., dogs) that live in and around human habitations, acting as a reservoir of infection.

Pulicide: An agent that kills members of the family Pulicidae, specifically fleas, used for flea control.

Problem-oriented medical diagnosis: A system of diagnosis that identifies and focuses on a patient's specific health problems, by considering potential causes (differential diagnoses) of each clinicopathological abnormality (problem) detected from the history, physical examination, and from laboratory and ancillary test results.

Schengen Agreement: A treaty signed in 1985 between five of the then ten member states of the European Economic Community near the town of Schengen in Luxembourg that led to the creation of Europe's borderless Schengen Area in 1995.

Signalment: That part of the veterinary medical history dealing with the animal's age, sex and breed.

Stealth organism: A microorganism that is difficult to detect using routine laboratory diagnostic tests.

Thrombocytopenia: A decrease in the number of platelets in circulating blood.

Box 1. CVBD World Forum Recommendations for the Management of CVBDs (from [7])
Forget about "exotic disease"
Stay abreast of latest research
Prevention is the best approach
Fleas are more than just a nuisance
Sand flies are the only proven vector of leishmaniosis, but in non-endemic areas vets should be aware of non-vectorial routes of transmission
Know the travel schedule of your clients
As diagnosis can be complex and challenging, consider all options
Understand that treatment may not be the end of the story
Engage with your clients to improve outcomes
Alert public health authorities where appropriate

Figure legends

Figure 1. *Rhipicephalus sanguineus* ticks in the ear **(A)** and between the toes **(B)** of a dog. In addition to disease transmission, *R. sanguineus* ticks cause anaemia, skin disease, and debilitation of dogs. (B) used with permission from [80].

Figure 2. *Ctenocephalides felis* (the cat flea), vector of significant zoonoses including bartonellosis and flea-borne spotted fever. Image courtesy of iStockPhoto.

Figure 3. *Ixodes holocyclus*, the Australian paralysis tick, attached to the scalp of a human (Image: Dr. Stephen Doggett).