Veterinary Parasitology 251 (2018) 68–77

Contents lists available at ScienceDirect

Veterinary Parasitology

journal homepage: www.elsevier.com/locate/vetpar

Review article

Arthropod-borne pathogens of dogs and cats: From pathways and times of transmission to disease control

Domenico Otranto*

Dipartimento di Medicina Veterinaria, Università degli Studi di Bari, 70010, Valenzano, Italy

ARTICLE INFO

Keywords:
parasites
Vectors
Arthropod-borne pathogens
Dog
Cat
Emerging
Zoonoses
Control

ABSTRACT

Vector-borne pathogens have developed a close relationship with blood feeding arthropod ectoparasites (e.g., mosquitoes, ticks, phlebotomine sand flies, black flies, fleas, kissing bugs, lice) and exploited a huge variety of vector transmission routes. Therefore, the life cycles of these pathogens result in a long evolved balance with the respective arthropod biology, ecology and blood feeding habits, instrumentally to the infection of several animal species, including humans. Amongst the many parasite transmission modes, such as ingestion of the arthropod, with its faeces or secretions, blood feeding represents the main focus for this article, as it is a central event to the life of almost all arthropod vectors. The time frame in which pathogens are transmitted to any animal host is governed by a large number of biological variables related to the vector, the pathogen, the host and environmental factors. Scientific data available on transmission times for each pathogen are discussed relative to their impact for the success of vector-borne disease control strategies. Blocking pathogen transmission, and thus preventing the infection of dogs and cats, may be achievable by the use of chemical compounds if they are characterised by a fast onset of killing activity or repellence against arthropods. The fast speed of kill exerted by systemic isoxazoline, as well as the repellent effect of pyrethroids have renewed the interest of the scientific community and pharmaceutical companies towards reducing the burden of vector-borne diseases under field conditions. However, endosymbionts and vaccines targeting arthropods or pathogen antigens should be further investigated as alternative strategies towards the goal of achieving an effective integrated control of vector-borne diseases.

1. Arthropod parasites: the perk of being a blood feeder

We do know that any organism living at the expenses of another (the host), by feeding, inhabiting on/in the host, or exploiting its biological, ecological and metabolic patterns has a name: parasite. Amongst ectoparasites, blood feeding arthropods represent the "epitome" of heterotrophic organisms. Literally, the term "parasite", refers to the action of feeding at the expenses of its host (from Greek: para- (beside) + sitos (wheat and, lately, food). Among the ancients, this term was sacred and it referred to a comic mask (in Hellenistic and Roman theatre), a character that used to feed at the table of the master/lord (…the host). From its original meaning of a hanger-on, scrounger, the term parasite has been transferred to any living creature which lives and feeds at the expenses of another having as priority to ensure the survival of their host. Therefore, feeding is an important concept to be explored (at a cellular, individual and even population level) in any parasite-host interaction, while this interaction is usually optimised by the parasite in an attempt to survive without causing major harm to the host. In the case of vector-borne diseases (VBD), pathogens transmitted by vectors have hijacked the biology, ecology and blood feeding habits of arthropods, establishing a close relationship with the latter, which is instrumental to the infection and survival in the final host. A further level of parasitism (in some cases mutualism) is established with endosymbiont bacteria in arthropods and/or in pathogens. Therefore, the arrays of vector-borne transmission pathways represent one of the most fascinating, and complex, example of evolution/interaction among pathogens, hosts and vectors, evolved under the pressure of a range of ecological and environmental drivers (Combes, 2001). The need for blood meals from a host in order to produce egg batches (i.e. anautogeny) emphasizes the obligate parasitic existence some arthropods have developed, laying a significantly larger number of eggs than unfed ones (Attardo et al., 2005). Several bacteria, viruses, protozoa and helminths have taken advantage of the biology of blood feeders to ensure their transmission and distribution to receptive hosts, both at individual and population level. Undoubtedly, knowledge of the feeding habits of arthropod vectors, as well as the array of ecological and environmental factors influencing the interactions between them, the pathogens transmitted and the hosts are of paramount importance in medical and

* Corresponding author.
E-mail address: domenico.otranto@uniba.it.

https://doi.org/10.1016/j.vetpar.2017.12.021
Received 12 November 2017; Received in revised form 25 December 2017; Accepted 26 December 2017

veterinary sciences (Otranto and Wall, 2008). This is not only a fascinating field of study in parasitology, but it is pivotal for exploring future strategies for controlling VBD and for understanding the reasons of some failure to achieve control (e.g., vaccines against arthropods). Here some of the processes are discussed, which occur during arthropod blood meal, favouring pathogen transmission and the potential control for VBD of dogs and cats with a focus on those of zoonotic concern. From the appreciation of the arthropod-host-pathogen interactions to the VBD control, may be just a small step further.

2. Zoonotic vector-borne diseases

VBD greatly impact human health as they cause around 1 million deaths annually (Hotez, 2014; WHO, 2016), and their importance in veterinary medicine also lies in the increasingly close relationship that domestic animals have established globally with humans, at any latitude and in any socio-economic context, from the poorest to the richest (Dantas-Torres and Otranto, 2014). VBD with anthroponotic (i.e., from human to human) cycles have had a major impact in the history of humankind (plague, yellow-fever, malaria, louse-borne typhus and louse-borne relapsing fever) and they have been well studied (Cox, 2002; Pages et al., 2010). Due to improvement of nutritional and health conditions during the post-industrial revolution and to the availability of chemotherapeutics (e.g., quinine derivate), many of the above VBD, such as malaria, became "curable illnesses" in developed countries, remaining a major threat only in the poorest, developing contexts (Pages et al., 2010). The perspectives for eradication of these diseases are promising as, for example, WHO Global Strategy for Malaria (2016–2030) set the ambitious global target to reduce malaria case incidence and mortality by at least 90% by 2030, eliminating malaria in 35 endemic countries.

However, the abundance of blood feeding insects (e.g., Ceratopogonidae, Simulidae, Pulicidae, Reduviidae, Culicidae, Psychodidae) and/or arachnid vectors (e.g., Ixodidae, Argasidae), the poor conditions of some human populations (malnourished, low hygienic standard) and the insalubrity of the environment, remain major drivers for the distribution of VBD, being a paradigmatic example of how the "One Health" concept needs to be applied in managing the great variety of infections. Many VBD are zoonotic, being transmitted from vertebrate animals to humans, and vice versa. These infections are caused by a wide range of viruses (e.g., Crimean-Congo haemorrhagic fever virus, West Nile virus, tick-borne encephalitis virus), bacteria (e.g., *Rickettsia conorii*, *Rickettsia rickettsii*, *Borrelia burgdorferi* sensu lato), protozoa (e.g., *Babesia divergens*, *Babesia microti*, *Leishmania infantum*, *Plasmodium knowlesi*, *Trypanosoma cruzi*) and helminths (e.g., *Dirofilaria immitis*, *Dirofilaria repens*, *Onchocerca lupi*, *Thelazia callipaeda*) (Colwell et al., 2011; Dantas-Torres et al., 2012; Kilpatrick and Randolph, 2012; Otranto et al., 2013). The increase in dog and cat populations and their co-habitation with humans in urban and rural environments poses new threats to human health (Colwell et al., 2011; Otranto, 2015). Both stray and owned dogs and cats, if not properly treated with endo- and ectoparsiticides, are most likely exposed to pathogen transmission by vectors and can become competent reservoirs of pathogens (Otranto et al., 2017). In addition, free-ranging stray and sheltered dogs represent an important risk factor for VBD transmission in areas with high vector density. It is the case of pathogens such as *L. infantum,* whose cases are increasing in previously non-endemic geographical areas, due to a complex range of biological (e.g., occurrence of sand fly vectors, infective biting rates and occurrence of reservoirs hosts) and environmental factors (e.g., climate, dog travelling with their owners to endemic areas for vacation and rescue dog relocation from southern to central and northern Europe) (Maia and Cardoso, 2015). Again, previously unknown infectious agents (e.g., *O. lupi*) or emerging pathogens (e.g., *D. repens*) are being increasingly reported in humans and dogs worldwide (Colwell et al., 2011; Otranto et al., 2013) and their control is often impaired by the limited scientific knowledge of these parasites. Therefore, information on the biology, epidemiology of pathogens in vectors and hosts, and the complex processes of their transmission to receptive hosts is pivotal.

3. Transmission modalities and times

Vector-borne pathogens have exploited a number of ways to infect vertebrate hosts by "synchronizing" their biology and ecology with that of arthropod vectors. Indeed, arthropods may act as an ideal environment for parasite to multiply (if protozoa) or to evolve into the infective stage (if helminths) and, finally, to transfer into the host. The majority of VBD-causing pathogens affecting animals, including dogs, are transmitted by hematophagous arthropods (e.g., mosquitoes, ticks, sand flies and fleas) through the blood meal of females, that need protein components as nutrients for their gonadotrophic cycles. The amount of blood imbibed largely varies according to the arthropod species from 1 µl or less in sand flies (Daba et al., 2004), to 2–6 µl in mosquitoes (Clements, 1992) up to 1.780 ml in *Amblyomma hebraeum* ticks (Rechav et al., 1994). Ticks can ingest blood 200–600 times their unfed bodyweight with the largest amount of imbibed blood ever reported (i.e., 8.856 ml) in an individual *Hyalomma asiaticum* tick (in Sonenshine and Roe, 1993). Other ways of pathogen transmission by arthropods is through their faeces (e.g., *T. cruzi* by triatominae bugs), ingestion (*Hepatozoon canis* and *Hepatozoon americanum* with ticks; *Dipylidium caninum* with fleas and lice) or when they feed on lachrymal secretions (*T. callipaeda* by zoophilic secretophagous flies) (Otranto et al., 2006; Baneth, 2011). In the latter case, these drosophilid flies (only males) display an unusual behavioural pathway feeding on animal secretions (Fig. 1), which has been argued to represent an evolving tendency towards parasitism (Máca and Otranto, 2014). However, blood feeding is the most important modality for pathogen transmission, being, in most of the cases, an active process, such in the case of most pathogens transmitted by mosquitoes, fleas, sand flies and ticks (Schorderet-Weber et al., 2017). An exception is represented by *D. immitis*, with third stage larvae of this filarioid regurgitated by the mosquitoes and penetrating in the lesioned skin surface (Simón et al., 2012).

Though a better understanding of the biology, mechanisms and timing of pathogen transmission could provide interesting clues for the control of VBD, information about these modalities is still limited to laboratory reports (Kidd and Breitschwerdt, 2003; Little et al., 2007; Fourie et al., 2013a; Saraiva et al., 2014). Overall, it is clear that the inoculation of any pathogen into a host does not imply that it shall succeed in establishing, through its multiplication (infection), eventually, causing disease (Fig. 2). Pathogen transmission times are governed by a large number of biological variables related to the vectors, the pathogens and the host immune responses (de la Fuente et al.,

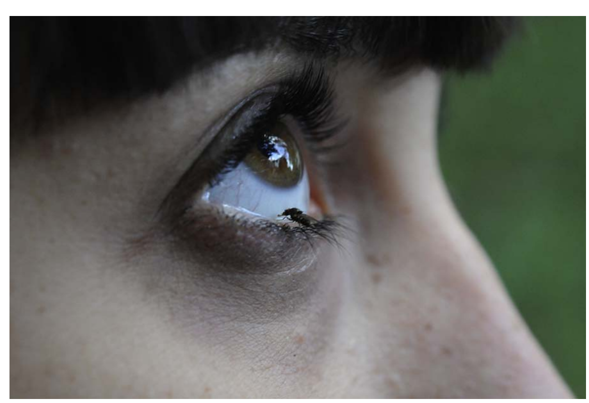

Fig. 1. *Phortica variegata* (Drosophilidae, Steganinae) fly feeding on eye secretions of a person in the Basilicata region (Southern Italy), a highly endemic area for *Thelazia callipaeda*. This fly species exhibits a zoophilic behavior (it feeds on vegetable substrate and also on lachrymal secretions of humans and carnivores) and it is vector of the eyeworm *T. callipaeda* in Europe.