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***Anaplasma*, *Ehrlichia*, *Rickettsia* infections in cats: European guidelines from the ABCD on prevention and management**

Pennisi M.G.¹, Hofmann-Lehmann R., Radford A.D., Tasker S., Belak S., Addie D., Boucraut-Baralon C., Egberink H., Frymus T., Gruffydd-Jones T., Hartmann K., Horzinek M.C., Hosie M.J., Lloret A., Lutz H., Marsilio F., Thiry E., Truyen U., Möstl K.

Synopsis

Anaplasma spp., *Ehrlichia* spp. and *Rickettsia* spp. are vector-borne pathogens infecting many mammalian species, but causing disease in very few of them. *Anaplasma phagocytophilum* is the most important feline pathogen among them and co-infections are possible.

Some species (*A. phagocytophilum*, *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Rickettsia conorii*, *Rickettsia rickettsii*, *Rickettsia felis*, *Rickettsia typhi*) are of zoonotic concern.

The geographical distribution of *Anaplasma*, *Ehrlichia* and *Rickettsia* pathogens overlaps with that of their competent vectors (ticks or fleas).

Little information is available on the pathogenesis of these agents in cats.

Clinical signs are usually reported soon after tick infestation. They are mostly non-specific and consist of fever, anorexia, lethargy. Joint pain may occur.

Blood or buffy-coat smear evaluation may be useful for cytological diagnosis of infections with *Ehrlichia* and *Anaplasma* spp.

¹ Corresponding author

Antibodies to rickettsial infections can be detected by immunofluorescence (IF) test and ELISA, but cross-reactions exist between organisms of the same genus.

Blood PCR analysis is a sensitive and specific method for confirming diagnosis at the onset of acute clinical signs before starting therapy when antibody testing is usually still negative.

Doxycycline is the first choice antibiotic for treating rickettsial infections.

Regular application of appropriate ectoparasiticide spot on or collars protects cats from infection.

In endemic areas blood donors should be tested for rickettsial blood-borne infections.

Infected cats are “sentinels” of the presence of rickettsial pathogens in ticks and fleas in a given geographical area and they signal a risk for people exposed to vectors.

Direct contact with cat saliva should be avoided because of the potential contamination by *R. felis* as well as by other zoonotic pathogens.

Agent properties and epidemiology

Obligate intracellular Gram negative coccoid organisms of the *Anaplasma*, *Ehrlichia* and *Rickettsia* genera are vector-borne members of the *Rickettsiales* order infecting humans and a wide variety of domestic and wild animals worldwide (Allison and Little, 2013). They generally have a wide host specificity, considering that many mammalian species can be infected. Importantly, some hosts might serve as reservoirs of infection; however, susceptibility to disease is usually more restricted.

Anaplasma, *Ehrlichia* and *Rickettsia* are difficult to culture *in vitro*; molecular genetics opened new avenues to study their infection biology (Allison and Little, 2013).

Compared to dogs, these pathogens have been generally less studied in cats (Table 1).

Table 1: Members of the *Ehrlichia*, *Anaplasma* and *Rickettsia* genera detected in cats in various countries. Please note that the rickettsial infections may occur even in additional countries, however, not published so far. Therefore it is possible that cats are infected in a larger range of countries, not listed in this table, particularly in areas where the competent tick vectors are abundant (see the text).

<i>Ehrlichia</i> genus	Countries in which the infection has been detected
<i>E. canis</i>	Canada USA Brazil Portugal
<i>E. chaffeensis</i>	USA Brazil
<i>E. ewingii</i>	USA
<i>Ehrlichia</i> spp.	Italy USA Kenia France
<i>Anaplasma</i> genus	
<i>A. phagocytophilum</i>	USA Sweden Finland Poland Switzerland Germany Italy Spain
<i>A. platys</i>	USA Brazil
<i>A. platys</i> -like	Italy
<i>A. bovis</i>	Japan
<i>Rickettsia</i> genus	
<i>R. rickettsii</i>	USA
<i>R. conorii</i>	Spain
<i>R. massiliae</i>	Spain
<i>Rickettsia</i> spp.	Italy

Anaplasma and *Ehrlichia* spp. are tick-borne pathogens of the *Anaplasmataceae* family and are pleomorphic intravacuolar organisms that replicate in haemopoietic cells. They give rise to cytoplasmic inclusion bodies: small elementary bodies (0.2-0.4 μm diameter), larger reticulate bodies and *morulae* (up to 2-6 μm).

Anaplasma phagocytophilum replicates in myeloid cells (mostly in neutrophils; Fig. 1) and is the agent of granulocytotropic anaplasmosis. It infects persons and a wide range of animal species worldwide, especially in the Northern hemisphere. It is the most important feline pathogen of the *Anaplasma* genus. Wild small mammals are the natural reservoirs. Antibody prevalence to *A. phagocytophilum* in cats has been reported as 4.5-33.3% in Italy (Ebani and Bertelloni, 2014; Persichetti et al., 2016), 2.0-8.0% in Spain (Solano-Gallego et al., 2006; Ayllón et al., 2012), 16.2% in Germany (Hamel et al., 2012), 22.1% in Sweden (Elfving et al., 2015) and 1.8-38.0% in the USA (Magnarelli et al., 2005; Billeter et al., 2007; Hegarty et al., 2015). *Anaplasma phagocytophilum* DNA was recently amplified in 0.4% of blood samples from cats admitted to veterinary clinics in South Germany (Bergmann et al., 2015).

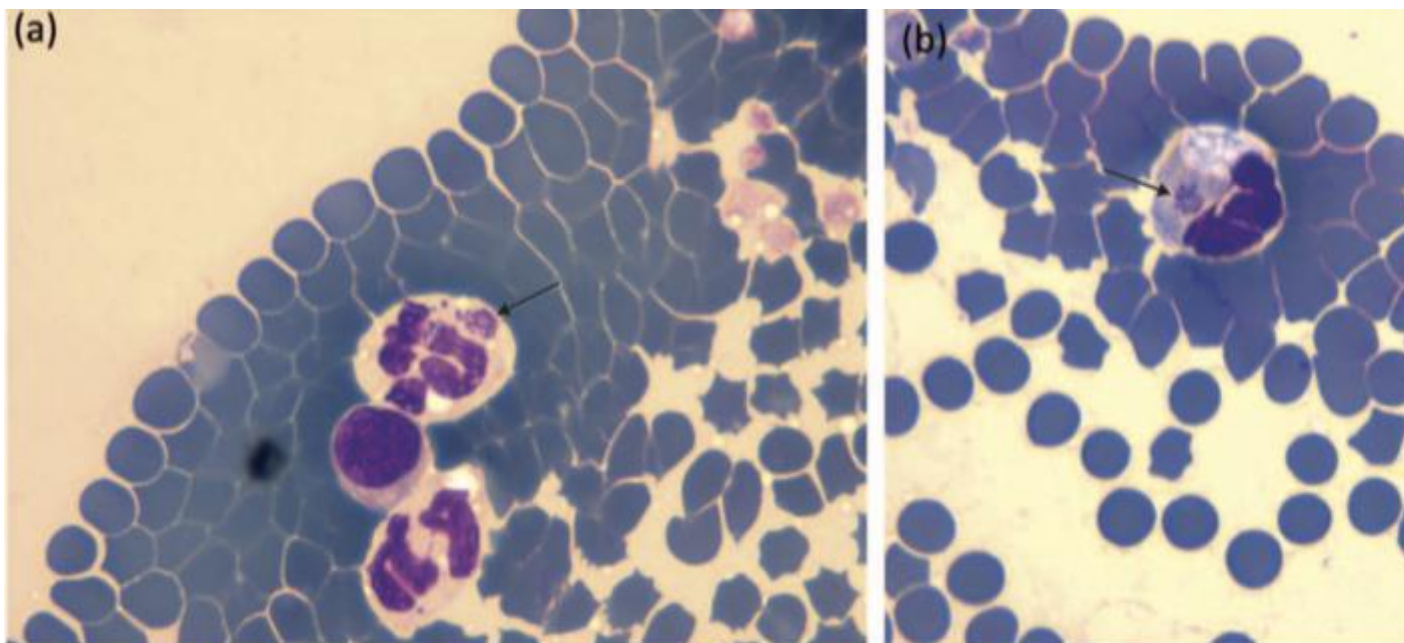


Fig. 1. Presence of *Anaplasma* spp *morulae* (arrows) in neutrophils. Reprinted with permission from Adaszek et al., 2013.

Anaplasma platys replicates in mature platelets and is the agent of thrombocytotropic anaplasmosis, a disease well documented worldwide in dogs (Sainz et al., 2015). In cats, it has been occasionally detected by PCR analysis (Lima et al., 2010; Qurollo et al., 2014; Hegarty et al., 2015). *Anaplasma bovis* has also been found by PCR in feline blood samples from Japan (Sasaki et al., 2012). Recently a novel, unclassified *A. platys*-like strain from cats was characterized in Sardinia (Italy). This strain, despite its tropism for platelets, is closely related to others identified in ruminants (Zobba et al., 2015).

Ehrlichia canis is the agent of canine monocytotropic ehrlichiosis. This disease was described in tropical and temperate areas worldwide, with the exception of Australia. *Ehrlichia chaffeensis* is the agent of human monocytotropic ehrlichiosis reported mainly from the USA. The granulocytotropic *Ehrlichia ewingii* has been evidenced in dogs and humans in the Midwestern and Southern United States. *E. canis* has been detected by PCR in blood samples from cats (Breitschwerdt et al., 2002; Oliveira et al., 2009; Ayllón et al., 2012; Braga et al., 2012, 2013, 2014; Maia et al., 2014; Hegarty et al., 2015; André et al., 2015). Less frequently, *E. chaffeensis* and *E. ewingii* were found (Braga et al., 2012; Hegarty et al., 2015). Cats seropositive for *E. canis* (6.0-18.0%) have been reported in Europe (Aguirre et al., 2004; Ortuño et al., 2005; Solano-Gallego et al., 2006; Ayllón et al., 2012; Ebani and Bertelloni, 2014; Persichetti et al., 2016), 5.5% in Brazil (Braga et al., 2012) and 0.7% in the USA (Hegarty et al., 2015).

Another member of the *Anaplasmataceae* family that leads to Neoehrlichiosis is '*Candidatus Neoehrlichia mikurensis*' (genus '*Candidatus Neoehrlichia*'). This emerging tick-borne agent has been found mainly in immunocompromised patients, in ticks and rodents and recently also in two dogs (Diniz et al., 2011; Hofmann-Lehmann et al., 2016), but so far not in cats. The infection may be underdiagnosed because diagnostic assays are not yet widely available.

The *Rickettsiaceae* family includes the spotted fever group (SFG) and the typhus group agents (Allison and Little, 2013). More than 20 species are included in the SFG

of the *Rickettsia* genus, some of them being important human pathogens. Historically, the most important zoonotic agents are *R. conorii* (the cause of Mediterranean spotted fever) in the Old World, and *R. rickettsii* (the agent of Rocky Mountains spotted fever) in the Americas. However, recent molecular studies have increasingly focused on other rickettsial species that may be involved in human clinical disease manifestations. *Rickettsia massiliae* for example is now recognised as the most widely distributed *Rickettsia* species that affects humans, being found worldwide (Brouqui et al., 2007).

Rickettsia rickettsii and *R. conorii* are both transmitted by ticks, infect dogs and may cause a clinical condition in dogs. Less information is available about the effect of these agents in cats. Feline infections caused by *R. massiliae* and *R. conorii* have been confirmed by both PCR and antibody testing in endemic areas of Spain and Portugal (Solano-Gallego et al., 2006; Alves et al., 2009; Vilhena et al., 2013; Segura et al., 2014), whereas cats seropositive for *R. rickettsii* have been reported in the USA (Case et al., 2006).

Rickettsia felis is worldwide an emerging flea-borne SFG human pathogen frequently detected in *Ctenocephalides felis*, less often in other flea species (Brouqui et al., 2007). *C. felis* is the vector and the recognised reservoir of *R. felis*, which is vertically transmitted to successive generations of fleas (Wedincamp and Foil, 2002). Recent studies carried out in some parts of Europe have shown that *Ctenocephalides* infection rates range from 2.8% in Albania (Silaghi et al., 2012) to 54.2% in Andalusia (Márquez et al., 2006). Cats are susceptible to *R. felis* infection and seroconvert after exposure to infected fleas. However, they are probably no reservoir hosts because of a short-term bacteraemia, with blood PCR testing usually negative in antibody positive cats (Wedincamp and Foil, 2000; Hawley et al., 2007; Segura et al., 2014; Persichetti et al., 2016). In rare cases, *R. felis* DNA can be amplified also from the skin or gingiva of cats, blood PCR testing being negative (Lappin and Hawley, 2009). It is unknown whether *R. felis* is present in other tissues of seropositive cats and whether it should be considered to be a feline pathogen.

Rickettsia typhi is a worldwide flea-borne rickettsia of the typhus group. It is the agent of murine or endemic typhus transmitted from rats by *Xenopsylla* fleas, or from cats to humans by *C. felis*, as well as to cats or wild animal reservoirs.

Just as in humans and dogs, co-infections with multiple vector-borne pathogens occur in cats; the consequences of such mixed infections are unknown (Maia et al., 2014; Qurollo et al., 2014; Hegarty et al., 2015; Lappin et al., 2015).

The geographical distribution of *Anaplasma*, *Ehrlichia* and *Rickettsia* pathogens overlaps with that of their competent vectors. In Europe, two tick species are mainly involved: *Rhipicephalus sanguineus* sensu lato, which is the main tick vector of *E. canis* and *R. conorii* (and suspected for *A. platys*); and *Ixodes ricinus*, the vector of *A. phagocytophilum*. Both species are found also on cats (Jameson and Medlock, 2011; Claerebout et al., 2013; Pennisi et al., 2015a).

Ixodes ricinus has a wide distribution, from the Mediterranean area to Scandinavian countries, and from Portugal to Ukraine (<http://ecdc.europa.eu/en/healthtopics/vectors/vector-maps/Pages/VBORNET-maps-tick-species.aspx>). In the Eastern part of Europe a closely related species, *Ixodes persulcatus* is found (Sainz et al., 2015). *Rhipicephalus sanguineus* sensu lato (the brown dog tick or kennel tick) is common in the Mediterranean basin; in northern countries, *R. sanguineus* is not indigenous but it can hibernate sheltered in cracks of kennel structures so that the area of its distribution is expanding northward.

In summary, *E. canis* and *A. platys* are considered endemic in Mediterranean countries but are spreading northward, whereas *A. phagocytophilum* is reported mainly in Northern and Central Europe (Sainz et al., 2015). In stray cats in Northern Italy, blood PCR for *A. phagocytophilum*, *Ehrlichia* spp. and *Rickettsia* spp. tested positive in 17.7%, 5.4% and 31.9%, respectively (Spada et al., 2014). Similar rates were found in healthy cats as compared to those showing clinical signs. Blood transfusion consequently may be a nonvectorial mode of transmission for rickettsial agents in cats, as it is well known in dogs (Sainz et al., 2015).

Pathogenesis and clinical signs

Little information is available on the pathogenesis of these agents in cats. A limited number of studies on experimental infections or exposure with *A. phagocytophilum* or *R. felis* in cats exist. Intraperitoneal experimental infection with *A. phagocytophilum* infected blood in a small number of cats resulted in a mild disease with transient fever not associated with changes in appetite or general appearance. However, mild reduction in total leukocyte, neutrophil and lymphocyte counts, remarkable reduction in PCV values, and transient increase of ALT and AST values were detected (Foley et al., 2003). Anti-nuclear antibodies and increased expression of γ IFN mRNA were also found in infected cats but they had normal antibody responses to FHV and FeLV vaccination two weeks post infection (p.i.). When experimental infection with *A. phagocytophilum* was performed in FIV-infected cats, upregulation of IL-10 expression was observed instead of γ IFN, but the clinical course of disease was similar (Foley et al., 2003). The recent experimental exposure of four cats with wild-caught adult *Ixodes scapularis* induced a quite subclinical dual infection with *A. phagocytophilum* and *Borrelia burgdorferi* (Lappin et al., 2015). In fact, a transient lymphopenia was the only abnormality detected during 13 weeks of observation after tick infestation, concerning general appearance, appetite, body temperature and cell blood count of the experimental cats (Lappin et al., 2015).

In naturally exposed cats, clinical signs of feline granulocytotropic anaplasmosis are usually reported soon after tick infestation. They are mostly non-specific and consist of fever, anorexia, lethargy and dehydration. Clinico-pathological abnormalities include mild or moderate thrombocytopenia, anaemia and lymphopenia (Bjöersdorff et al., 1999; Lappin et al., 2004; Schaarschmidt-Kiener et al., 2009; Heikkilä et al., 2010; Adaszek et al., 2013; Savidge et al., 2015). Lameness and swollen joints, epistaxis or pain on abdominal palpation were less frequently reported (Bjöersdorff et al., 1999; Tarello, 2005; Adaszek et al., 2013). The clinical course is usually short and not severe and abnormalities resolve quickly, particularly when antibiotic treatment is given.

Natural infection with *A. platys* in a cat in Brazil was associated with anorexia, lethargy, concurrent urinary infection and thrombocytopenia (Lima et al., 2010). In

another cat persistent *A. platys* infection was found concurrently with *Bartonella henselae*, *B. koehlerae* and *Candidatus Mycoplasma haemominutum* infections and the cat was also affected by multiple myeloma (Qurollo et al., 2014). In both cases, the pathogenic role of *A. platys* was not clearly established. In the cat with multiple myeloma, immunosuppression due to a severe monoclonal gammopathy could have been responsible for increased susceptibility to the co-infections.

Experimental subcutaneous inoculation of cats with a canine strain of *E. canis* was not successful and the pathogenesis of feline monocytotropic ehrlichiosis in cats is not known (Lappin and Breitschwerdt, 2012). The natural disease has been confirmed by molecular testing only in a few cases and mainly manifests as non-specific signs such as fever, anorexia and lethargy, but more rarely hyperesthesia, joint pain, pale mucous membranes, lymph node and spleen enlargement, and haemorrhagic diathesis (petechiae, vitreous haemorrhage) have also been reported (Lappin and Breitschwerdt, 2012). Haematology can reveal non-regenerative anaemia, thrombocytopenia, pancytopenia and increased or decreased white cell counts (Lappin and Breitschwerdt, 2012). Bone marrow hypoplasia is found in cats with pancytopenia or anaemia and thrombocytopenia on haematology (Breitschwerdt et al., 2002). The most consistent biochemical abnormality seen with feline monocytotropic ehrlichiosis was hyperproteinaemia and polyclonal or monoclonal gammopathy, which is also typical of the chronic course of canine monocytotropic ehrlichiosis (Lappin and Breitschwerdt, 2012). Anti-nuclear antibodies were found in some cats and neutrophilic polyarthritis was diagnosed in a cat with joint signs (Breitschwerdt et al., 2002).

Rickettsia felis infection was evaluated in clinically ill cats, but no association was found between antibody positivity and fever and no febrile cat was found to be PCR positive for *R. felis* or *R. rickettsii* (Bayliss et al., 2009).

Another study has explored the associations between *Ehrlichia* spp. or *A. phagocytophilum* infections and anaemia, but no significant associations were detected (Ishak et al., 2006).

Diagnosis

The main indication for diagnostic investigations for Rickettsial diseases is a febrile syndrome affecting cats exposed to ticks in endemic areas, especially stray or outdoor pet cats not protected by the regular use of appropriate ectoparasiticides.

Blood or buffy-coat smear evaluation may be useful for cytological diagnosis of infections with *Ehrlichia* and *Anaplasma* spp. In general, intracytoplasmic inclusion bodies are more frequently found in granulocytotropic anaplasmosis than in monocytotropic ehrlichiosis. *Anaplasma phagocytophilum* inclusion bodies are found in 1-24% of circulating neutrophils in cats with natural granulocytotropic anaplasmosis. In experimentally infected cats they appear 7-9 days p.i. (Foley et al., 2003) or over the first 10 weeks after tick infestation (Lappin et al., 2015). After antibiotic therapy they are no longer visible (Bjöersdorff et al., 1999; Heikkilä et al., 2010; Lappin et al., 2015). With *A. platys*, bacteraemia is cyclical at 1 to 2-week intervals, with a higher percentage of circulating infected platelets occurring during the first cycles (Harvey et al., 1978).

Antibodies to rickettsial infections can be detected by immunofluorescence (IF) test and ELISA. Cross-reaction is possible between *A. phagocytophilum* and *A. platys* but not with *E. canis*, although *E. canis* can cross react with other *Ehrlichia* spp. Antibodies against *A. phagocytophilum* were detected in an experimental study within 14 days p.i. and seroconversion occurs in natural infections even in antibiotic treated cats (Foley et al., 2003). In cats experimentally exposed to infected ticks, antibodies against *A. phagocytophilum* appeared 2-6 weeks after infestation (Lappin et al., 2015). In the case of a positive IF test at first sampling, a 4-fold increase of the titre over four weeks may confirm the acute course of the infection (Bjöersdorff et al., 1999; Foley et al., 2003; Lappin et al., 2004; Heikkilä et al., 2010). Some cats testing positive to *E. canis* by PCR were found to be antibody negative despite the chronic course of their disease suggesting that a negative antibody test does not exclude the diagnosis in cats with compatible clinical signs (Breitschwerdt et al., 2002).

Blood PCR analysis is a sensitive and specific method for confirming diagnosis at the onset of acute clinical signs when antibody testing is usually still negative (Foley et al., 2003; Lappin et al., 2015). Because of overlapping clinical signs, the use of genus-inclusive primers for *Ehrlichia–Anaplasma* and *Rickettsia* spp. genera in PCRs has been suggested followed by sequencing of any resulting PCR products to determine the infecting species (Allison and Little, 2013). However, a recent study demonstrated that some genus-specific PCRs also detect *Pseudomonas* sequences and may lead to false positive results that may only be recognized after sequencing analysis (Hofmann-Lehmann et al., 2016). Alternatively, the use of species-specific real-time TaqMan assays may be faster and more sensitive options for the molecular detection of rickettsaemia. Samples for microscopic detection or PCR should be collected prior to the initiation of antibiotic treatment.

Treatment

Doxycycline is the first choice antibiotic for treating rickettsial infections. It is administered at 10 mg/kg orally q24 for 28 days. Clinical improvement is seen in the first 24-48 hours unless co-infections not susceptible to doxycycline are present such as protozoal vector-borne agents, or if other complications develop such as severe bleeding. Animals generally respond well to treatment but may remain persistently infected.

In cases testing negative by microscopy, PCR or antibody test, or if results are not yet available, but where there is a strong clinical suspicion of rickettsial infections, treatment should be initiated to prevent the potential of rapid progression of clinical disease.

Prevention

As vectors are the main routes of transmission of rickettsial infections, regular application of appropriate ectoparasiticide spot on or collars may protect cats from becoming infected, as it is well recognised in dogs.

In endemic areas, blood donors should be tested for rickettsial blood-borne infections to confirm they are negative before being used as donors (Pennisi et al., 2015b).

Recommendations to avoid zoonotic transmission

Rickettsial pathogens are transmitted to humans by competent vectors. Infected cats, as well as dogs, are “sentinels” of the presence of rickettsial pathogens in ticks and fleas in a given geographical area and they signal a risk for people exposed to vectors. Regular application of ectoparasiticides to pets reduces the risk of exposure of humans to vectors of rickettsial agents. Direct contact with cat saliva should be avoided because of the potential contamination by *R. felis* as well as by other zoonotic pathogens.

References

Adaszek L, Górna M, Skrzypczak M, Buczek K, Balicki I, Winiarczyk S (2013). Three clinical cases of *Anaplasma phagocytophilum* infection in cats in Poland. *J Feline Med Surg* 15: 333-337.

Aguirre E, Tesouro MA, Amusatequi I, Rodríguez-Franco F, Sainz A (2004). Assessment of feline ehrlichiosis in central Spain using serology and a polymerase chain reaction technique. *Ann N Y Acad Sci* 1026: 103-105.

Allison RW, Little SE (2013). Diagnosis of rickettsial diseases in dogs and cats. *Vet Clin Pathol* 42: 127-144.

Alves AS, Milhano N, Santos-Silva M, Santos AS, Vilhena M, de Sousa R (2009). Evidence of *Bartonella* spp., *Rickettsia* spp. and *Anaplasma phagocytophilum* in domestic, shelter and stray cat blood and fleas, Portugal. *Clin Microbiol Infect* 15 (S2): 1-3.

André MR, Herrera HM, Fernandes Sde J, de Sousa KC, Goncalves LR, Domingos IH, de Macedo GC, Machado RZ (2015). Tick-borne agents in domesticated and stray cats from the city of Campo Grande, state of Mato Grosso do Sul, Midwestern Brazil. *Ticks Tick Borne Dis* 6: 779-786.

Ayllón T, Diniz PPVP, Breitschwerdt EB, Villaescusa A, Rodríguez-Franco F, Sainz A (2012). Vector-borne diseases in client-owned and stray cats from Madrid, Spain. *Vector-borne and zoonotic diseases* 12: 143-149.

Bayliss D, Morris AK, Horta MC, Labruna MB, Radecki SV, Hawley JR, Brewer MM, Lappin MR (2009). Prevalence of *Rickettsia* species antibodies and *Rickettsia* species DNA in the blood of cats with and without fever. *J Feline Med Surg* 11: 266-270.

Bergmann M, Englert T, Stuetzer B, Hawley JR, Lappin MR, Hartmann K (2015). Prevalence of selected rickettsial infections in cats in Southern Germany. *Comp Immunol Microbiol Infect Dis* 42: 33-36.

Billeter SA, Spencer JA, Griffin B, Dykstra CC, Blagburn BL (2007). Prevalence of *Anaplasma phagocytophilum* in domestic felines in the United States. *Vet Parasitol* 147: 194-198.

Bjöersdorff A, Svendenius L, Owens JH, Massung RF (1999). Feline granulocytic ehrlichiosis – a report of a new clinical entity and characterization of the infectious agent. *J Small Anim Pract* 40: 20-24.

Braga M, André MR, Freschi CR, Teixeira MCA, Machado RZ (2012). Molecular and serological detection of *Ehrlichia* spp. in cats on São Luís island, Maranhão, Brazil. *Rev Bras Parasitol Vet* 21: 37-41.

Braga IA, Santos LG, Melo AL, Jaune FW, Ziliani TF, Girardi A, de Aguiar DM (2013). Hematological values associated to the serological and molecular diagnostic in cats suspected of *Ehrlichia canis* infection. *Rev Bras Parasitol Vet* 22: 470-474.

Braga IA, Santos LG, Ramos DG, Melo AL, Mestre GL, de Aguiar DM (2014). Detection of *Ehrlichia canis* in domestic cats in the central-western region of Brazil. *Brazilian Journal of Microbiology* 45: 641-645.

Breitschwerdt EB, Abrams-Ogg AC, Lappin MR, Bienzle D, Hancock SI, Cowan SM, Clouten JK, Hegarty BC, Hawkins EC (2002). Molecular evidence supporting *Ehrlichia canis*-like infection in cats. *J Vet Intern Med* 16: 642-649.

Brouqui P, Parola P, Fournier PE, Raoult D (2007). Spotted fever rickettsioses in southern and eastern Europe. *FEMS Immunol Med Microbiol* 49: 2-12.

Case JB, Chomel B, Nicholson W, Foley JE (2006). Serological survey of vector-borne zoonotic pathogens in pet cats and cats from animal shelters and feral colonies. *J Feline Med Surg* 8: 111-117.

Claerebout E, Losson B, Cochez C, Casaert S, Dalemans AC, De Cat A, Madder M, Saegerman C, Heyman P, Lempereur L (2013). Ticks and associated pathogens collected from dogs and cats in Belgium. *Parasite & Vectors* 6: 183.

Diniz PP, Schulz BS, Hartmann K, Breitschwerdt EB (2011). “*Candidatus* Neoehrlichia mikurensis” infection in a dog from Germany. *J Clin Microbiol* 49: 2059–2062.

Ebani VV, Bertelloni F (2014). Serological evidence of exposure to *Ehrlichia canis* and *Anaplasma phagocytophilum* in Central Italian healthy domestic cats. *Ticks and Tick-borne Diseases* 5: 668-671.

ECDC (European Centre for Disease Prevention and Control):
(<http://ecdc.europa.eu/en/healthtopics/vectors/vector-maps/Pages/VBORNET-maps-tick-species.aspx>)

Elfving K, Malmsten J, Dalin AM, Nilsson K (2015). Serological and molecular prevalence of *Rickettsia helvetica* and *Anaplasma phagocytophilum* in wild cervids

and domestic mammals in the central parts of Sweden. *Vector Borne Zoonotic Dis* 15: 529-534.

Foley JE, Leutenegger CM, Dumler JS, Pedersen NC, Madigan JE (2003). Evidence for modulated immune response to *Anaplasma phagocytophila* sensu lato in cats with FIV-induced immunosuppression. *Comp Immunol Microbiol Infect Dis* 26: 103-113.

Hamel D, Bondarenko A, Silaghi C, Nolte I, Pfister K (2012). Seroprevalence and bacteremia of *Anaplasma phagocytophilum* in cats from Bavaria and Lower Saxony (Germany). *Berl Munch Tierarztl Wochenschr* 125: 163-167.

Harvey JW, Simpson CF, Gaskin JM (1978). Cyclic thrombocytopenia induced by a Rickettsia-like agent in dogs. *J Infect Dis* 137: 182-188.

Hawley JR, Shaw SE, Lappin MR (2007). Prevalence of *Rickettsia felis* DNA in the blood of cats and their fleas in the United States. *J Feline Med Surg* 9: 258-262.

Hegarty BC, Qurollo BA, Thomas B, Park K, Chandrashekar R, Beall MJ, Thatcher B, Breitschwerdt EB (2015). Serological and molecular analysis of feline vector-borne anaplasmosis and ehrlichiosis using species-specific peptides and PCR. *Parasite & Vectors* 8: 320.

Heikkilä HM, Bondarenko A, Mihalkov A, Pfister K, Spillmann T (2010). *Anaplasma phagocytophilum* infection in a domestic cat in Finland: case report. *Acta Vet Scand* 52: 62.

Hofmann-Lehmann R, Wagmann N, Meli ML, Riond B, Novacco M, Joekel D, Gentilini F, Marsilio F, Pennisi MG, Lloret A, Carrapiço T, Boretti FS (2016). Detection of 'Candidatus Neoehrlichia mikurensis' and other *Anaplasmataceae* and *Rickettsiaceae* in Canidae in Switzerland and Mediterranean countries. *Schweiz Arch Tierheilkd* 158: 691-700.

Ishak AM, Radecki S, Lappin MR (2006). Prevalence of *Mycoplasma haemofelis*, "Candidatus Mycoplasma haemominutum", *Bartonella* species, *Ehrlichia* species,

and *Anaplasma phagocytophilum* DNA in the blood of cats with anemia. *J Feline Med Surg* 9: 1-7.

Jameson LJ, Medlock JM (2011). Tick surveillance in Great Britain. *Vector Borne Zoonotic Dis.* 11(4): 403-412.

Lappin MR, Breitschwerdt ER (2012). *Ehrlichia* spp. infection (feline monocytotropic ehrlichiosis). In Greene CE: Infectious diseases of the dog and cat. Elsevier, St Louis, Missouri, p. 238-241.

Lappin MR, Breitschwerdt EB, Jensen WA, Dunnigan B, Rha JY, Williams CR, Brewer M, Fall M (2004). Molecular and serological evidence of *Anaplasma phagocytophilum* infection in cats in North America. *J Am Vet Med Assoc* 225: 893-896.

Lappin MR, Chandrashekar R, Stillman B, Liu J, Mather TN (2015). Evidence of *Anaplasma phagocytophilum* and *Borrelia burgdorferi* infection in cats after exposure to wild-caught adult *Ixodes scapularis*. *J Vet Diagn Invest* 27: 522-525.

Lappin MR, Hawley J (2009). Presence of *Bartonella* species and *Rickettsia* species DNA in the blood, oral cavity, skin and claw beds of cats in the United States. *Vet Dermatol* 20: 509-514.

Lima MLF, Soares PT, Ramos CAN, Araújo FR, Ramos RAN, Souza IIF, Faustino MAG, Alves LCA (2010). Molecular detection of *Anaplasma platys* in a naturally-infected cat in Brazil. *Brazilian Journal of Microbiology* 41: 381-385.

Magnarelli LA, Bushmich SL, IJdo JW, Fikrig E (2005). Seroprevalence of antibodies against *Borrelia burgdorferi* and *Anaplasma phagocytophilum* in cats. *Am J Vet Res* 66: 1895-1899.

Maia C, Ramos C, Coimbra M, Bastos F, Martins A, Pinto P, Nunes M, Vieira ML, Cardos L, Campino L (2014). Bacterial and protozoal agents of feline vector-borne

diseases in domestic and stray cats from southern Portugal. *Parasite & Vectors* 7: 115.

Márquez FJ, Muniain MA, Rodríguez-Liebana JJ, Del Toro MD, Bernabeu-Wittel M, Pachón AJ (2006). Incidence and distribution pattern of *Rickettsia felis* in peridomestic fleas from Andalusia, Southeast Spain. *Ann N Y Acad Sci* 1078: 344-346.

Oliveira LS, Mourão LC, Oliveira KA, Agostini M, Oliveira AC, Almeida MR, Fietto LR, Conceição LG, Filho JDR, Galvão MAM, Mafra C (2009). Molecular detection of *Ehrlichia canis* in cats in Brazil. *Clin Microbiol Infect* 15(S2): 53-54.

Ortuño A, Gauss CB, García F, Gutierrez JF (2005). Serological evidence of *Ehrlichia* spp. exposure in cats from northeastern Spain. *J Vet B Infect Dis Vet Public Health* 52: 246-248.

Pennisi MG, Hartmann K, Addie DD, Lutz H, Gruffydd-Jones T, Boucraut-Baralon C, Egberink H, Frymus T, Horzinek MC, Hosie MJ, Lloret A, Marsilio F, Radford A, Thiry E, Truyen U, Möstl K (2015b). Blood transfusion in cats. ABCD guidelines for minimising risks of infectious iatrogenic complications. *J Feline Med Surg* 17: 589-593.

Pennisi MG, Persichetti MF, Serrano L, Altet L, Reale S, Gulotta L, Solano-Gallego L (2015a). Ticks and associated pathogens collected from cats in Sicily and Calabria (Italy). *Parasite & Vectors* 8: 512.

Persichetti MF, Solano-Gallego L, Serrano L, Altet L, Reale S, Masucci M, Pennisi MG (2016). Detection of vector-borne pathogens in cats and their ectoparasites in southern Italy. *Parasite & Vectors* 9: 247.

Qurollo BA, Balakrishnan N, Cannon CZ, Maggi RG, Breitschwerdt ER (2014). Co-infection with *Anaplasma platys*, *Bartonella henselae*, *Bartonella koehlerae* and 'Candidatus Mycoplasma haemominutum' in a cat diagnosed with splenic plasmocytosis and multiple myeloma. *J Feline Med Surg* 16: 713-720.

Sainz A, Roura X, Miró G, Estrada-Peña A, Kohn B, Harrus S, Solano-Gallego L (2015). Guideline for veterinary practitioners on canine ehrlichiosis and anaplasmosis in Europe. *Parasite & Vectors* 8: 75.

Sasaki H, Ichikawa Y, Sakata Y, Endo Y, Nishigaki K, Matsumoto K, Inokuma H (2012). Molecular survey of *Rickettsia*, *Ehrlichia*, and *Anaplasma* infection of domestic cats in Japan. *Ticks and Tick-borne Diseases* 3: 307-310.

Savidge C, Ewing P, Andrews J, Aucoin D, Lappin MR, Moroff S (2015). *Anaplasma phagocytophilum* infection of domestic cats: 16 cases from northeastern USA. *J Feline Med Surg* Feb 13. pii: 1098612X15571148.

Schaarschmidt-Kiener D, Graf F, von Loewenich FD, Müller W (2009). *Anaplasma phagocytophilum* infection in a cat in Switzerland. *Schweiz Arch Tierheilkd* 151: 336-341.

Segura F, Pons I, Miret J, Pla J, Ortuño A, Nogueras M-M (2014). The role of cats in the eco-epidemiology of spotted fever group diseases. *Parasite & Vectors* 7: 353.

Silaghi C, Knaus M, Rapti D, Kusi I, Shukullari E, Hamel D, Pfister K (2012). Survey of *Toxoplasma gondii* and *Neospora caninum*, haemotropic mycoplasmas and other arthropod-borne pathogens in cats from Albania. *Parasite & Vectors* 7: 62.

Solano-Gallego L, Hegarty B, Espada Y, Llull J, Breitschwerdt E (2006). Serological and molecular evidence of exposure to arthropod-borne organisms in cats from northeastern Spain. *Vet Microbiol* 118: 274-277.

Spada E, Proverbio D, Galluzzo P, Della Pepa A, Perego R, Bagnagatti De Giorgi G, Ferro E (2014). Molecular study on selected vector-borne infections in urban stray colony cats in northern Italy. *J Feline Med Surg* 16: 684-688.

Tarello W (2005). Microscopic and clinical evidence for *Anaplasma (Ehrlichia) phagocytophilum* infection in Italian cats. *Vet Rec* 156: 772-774.

Vilhena H, Martinez-Díaz V, Cardoso L, Vieira L, Altet L, Francino O, Pastor J, Silvestre-Ferreira AC (2013). Feline vector-borne pathogens in the north and centre of Portugal. *Parasite & Vectors* 6: 99.

Wedincamp J Jr, Foil LD (2000). Infection and seroconversion of cats exposed to cat fleas (*Ctenocephalides felis* Bouché) infected with *Rickettsia felis*. *J Vector Ecol*. 25:123-126.

Wedincamp J Jr, Foil LD (2002). Vertical transmission of *Rickettsia felis* in the cat flea (*Ctenocephalides felis* Bouché). *J Vector Ecol* 27: 96-101.

Zobba R, Anfossi AG, Visco S, Sotgiu F, Dedola F, Pinna Parpaglia ML, Battilani M, Pittau M, Alberti A (2015). Cell tropism and molecular epidemiology of *Anaplasma platys*-like strains in cats. *Ticks Tick Borne Dis* 6: 272-280.