

BARTONELLOSIS IN CATS AND ITS ROLE IN PUBLIC HEALTH

[*Bartonelose em gatos e sua importância na saúde pública*]

Camila Lopes Riberio de Almeida^{1*}; Veronica J. Babo-Terra²

1 Acadêmica de Medicina Veterinária da FAMEZ/UFMS. Av. Filinto Muller, 2443, Campo Grande, MS.

2 Profa Dra. de Clínica Médica e Terapêutica de Pequenos Animais da FAMEZ/UFMS. Av. Filinto Muller, 2443, Campo Grande, MS.

ABSTRACT - The genus *Bartonella* is composed of various zoonotic species that cause important diseases, usually in immunosuppressed individuals. The main reservoirs are domestic felines and these do not often present any clinical signs, but are usually in a state of intermittent bacteremia. So that, there is a potential risk of disease dissemination as well as transmission of the agent to other cats, mainly by the feces of fleas, and to human beings through the bite or scratch of the animal. The aim of this study was to review the occurrence of Bartonellosis in humans and cats, as well as the major zoonotic, clinical, laboratorial and treatment aspects. Further studies are necessary in order to gather more knowledge about the disease and its prevention. However, we have to point out that, since the definitive diagnosis and treatment in cats are still uncertain and controversial issues, the best way to control the disease is so far through the animal vector control, by the adoption of a correct and effective protocol of flea control, and by preventing bites and scratches in immunosuppressed people and professionals who directly deal with cat.

Keywords: Feline, humans, zoonosis.

RESUMO - O gênero *Bartonella* é composto por várias espécies que possuem caráter zoonótico e que causam doenças importantes, geralmente em pessoas imunossuprimidas. Os principais reservatórios são os gatos domésticos sendo que estes geralmente não apresentam sintomatologia, mas encontram-se, muitas vezes, em situação de bacteremia intermitente, de forma que existe o risco potencial de disseminação da doença e transmissão do agente para outros gatos, principalmente por meio das fezes das pulgas, e para o próprio homem, através da mordida ou da arranhadura do animal. O objetivo do estudo foi revisar a ocorrência de Bartonelose em humanos e em felinos, bem como principais aspectos zoonóticos, clínicos, laboratoriais e terapêuticos. Mais estudos precisam ser realizados com o intuito de aprofundar os conhecimentos referentes à doença bem como sua prevenção, porém, o que se deve ter em mente é que como o diagnóstico definitivo da enfermidade e o tratamento em gatos ainda são assuntos polêmicos e muito duvidosos, a melhor maneira de controlar a doença, até o momento, é por meio do controle dos vetores no animal, a partir da adoção de um protocolo de controle de pulgas correto e eficaz, bem como a prevenção de mordidas e arranhões em pessoas imunossuprimidas e profissionais que lidam diretamente com felinos.

Keywords: Felino, homem, zoonose.

INTRODUCTION

A new organism, *Rochalimaea henselae*, was discovered in 1992 (Regnery *et al.*, 1992a,b) and in the following year, Brenner *et al.* (1993) proposed the unification of genera *Rochalimaea* e *Bartonella* and, thereby, the bacterium was renamed *Bartonella henselae*. Since then, hundreds of articles have been published regarding treatment, clinical signs and epidemiology of the infection in humans and animals, especially in the domestic cat.

The genus *Bartonella* is constituted by various zoonotic species that represent emerging infectious diseases in Brazil and around the world (Chomel *et al.*, 2006; Breitschwerdt, 2008; Mogollon-Pasapera, 2009). Among them, *Bartonella henselae* is the most studied and reported to cause disease in humans (Boulouis *et al.*, 2005; Guptill, 2010). It's characterized as Gram negative fastidious bacillus that adhere to endothelial cells and erythrocytes after biting and/or cat-scratch, affecting mainly young animals less than a year of age (Breitschwerdt *et al.*, 2000; Chomel *et al.*, 2004; Boulouis *et al.*, 2005).

* Autor para correspondência: milalopes@hotmail.com

The most emerging diseases caused by *Bartonella* species were first described in humans and later in cats and dogs. Some studies demonstrated that pet cats serve as the main persistent reservoir host that shows prolonged asymptomatic bacteremia to five *Bartonella* species: *Bartonella henselae*, *Bartonella clarridgeiae*, *Bartonella koehlerae*, *Bartonella weissii* and *Bartonella elizabethae* (Kordick *et al.*, 1999; Breitschwerdt & Kordick, 2000; Breitschwerdt, 2008).

The aim of this study was to review the occurrence of Bartonellosis in humans and cats, as well as the major zoonotic, clinical, laboratorial and treatment aspects because, according to Kikuchi *et al.* (2002), although underestimated, the disease has great importance in Brazil and other countries.

REVIEW

BARTONELLOSIS IN PET CATS

Occurrence of the agent in cats in Brazil and other countries

In a study conducted in Northern California, researchers found a high prevalence of *Bartonella henselae* infections in young cats (Chomel *et al.*, 1995). The bacteria was isolated from blood of 39,5% (81/205) of the cats, which were subsequently confirmed by the PCR technique. Also 81% (166/205) of the animals had antibodies against the microorganism.

Another study conducted in the United States (Guptill *et al.*, 2004), demonstrated seropositivity, using the enzyme linked immunosorbent assay (ELISA), in 51% (138/271) of the cats, with the highest prevalence been detected in Florida (67%), when compared to other three studied regions (Southern California, metropolitan regions of Chicago and Washington).

In 2005, the first study about the prevalence of *B. henselae* in cats from Spain was conducted (Pons *et al.*, 2005). From the blood samples of 100 cats, culture was positive to seven and subsequent differentiation among species was performed by PCR test, which showed the presence of *B. henselae*. Subsequently, through the Indirect Immunofluorescence test, antibodies against the bacteria were found in 29,6% (34/115) of the cats.

In a research conducted in France, blood samples were collected from 94 stray cats. The material was cultivated and results showed a prevalence of 53% (50/94) of *Bartonella* spp. Then, using the PCR test on the growing material, the authors identified 70% (35/50) of positivity to *B. henselae* and 30% (15/50) related to *B. clarridgeiae*. Therefore, the importance of the cat as a reservoir for the bacteria was highlighted in this study (Heller *et al.*, 1997).

In Brazil, recent research in Rio de Janeiro state (Souza *et al.*, 2010) demonstrated high prevalence, through molecular biology, of *Bartonella* spp. in pet cats that lived in a shelter, in which from 37 animals studied, 36 (97,3%) were positive for the genus *Bartonella*.

In another analysis (Crissiuma *et al.*, 2011) in the same state, 40 healthy cats were tested showing 17 (42,5%) positive cases for *Bartonella* DNA species in the blood, detected by PCR test, and 19 (47,5%) presenting antibodies against the microorganism in the serum, through the Immunofluorescence test.

Another similar research carried out in Brazil, in Rio Grande do Sul state, detected *Bartonella* spp. in 17,02% (8/47) of the samples collected from 47 cats aged less than 12 months, using PCR. From the phylogenetic analysis by the DNA sequencing of the eight positive samples, five corresponded to *B. henselae* and three to *B. clarridgeiae* (Staggemeier *et al.*, 2010).

A recent research using PCR (Braga *et al.*, 2012) in 200 cats revealed nine cats (4,5%) positive for the genus *Bartonella*. In the same year, a study conducted in Sao Paulo, Jaboticabal city, revealed positivity of 4,3% among healthy cats, using PCR method (Bortoli *et al.*, 2012).

Transmission among cats

The primary way of transmission among cats is by fleas, especially *Ctenocephalides felis*. These fleas ingest the microorganism during blood meal in infected cats and, so that viable bacteria can be found in feces of the vector. The transmission to the vector occurs by contact with fleas or through their remaining feces in the animal's coat which contain live bacteria for at least nine days (Chomel *et al.*, 1996).

In a study conducted by Foil *et al.* (1998), cats became bacteremic after intradermal inoculation of

the contaminated flea feces. Thus, the infection of other cats and possibly humans may happen at the moment the cat scratches due to nails contamination by flea feces.

Studies have shown that an infected cat and an uninfected one can live together freely, as long as flea infestation doesn't occur; otherwise, transmission between cats happens easily. Besides, it was impossible to detect, in a free fleas environment, venereal transmission among bacteremic animals and among the queen and her kittens during the pregnancy and neonatal period (Abbot *et al.*, 1997; Guptill *et al.*, 1997; Guptill *et al.*, 1998). However, another study showed the possibility of transmitting the agent *B. henselae* by blood transfusions (Magalhães *et al.*, 2008).

Researchers also revealed the presence of bacterial DNA in ticks and hematophagous flies, showing that the role of other vectors in transmitting Bartonellosis should be further explored (Sanogo *et al.*, 2003; Chung *et al.*, 2004).

Clinical signs

Bartonellosis in cats is a controversial subject, once the majority of animals remain asymptomatic (Kordick *et al.*, 1997; AAFF, 2006). However, when cats show any symptoms, it is difficult to associate them to the disease itself as these may be nonspecific and mimic other diseases such as Feline Herpesvirus type 1, Feline Calicivirus, Feline Immunodeficiency virus and Feline Leukemia Virus (Quimby *et al.*, 2007; Dowers *et al.*, 2010). Under these circumstances, these disorders can mislead diagnosis, complicate treatment and prevention of transmission to other cats and humans.

Symptoms in cats, when they exist, are usually associated to upper and lower urinary tract infections, stomatitis and lymphadenopathy (Chomel *et al.*, 2006). However, some cases of uveitis and endocarditis have been associated, by molecular biology, to *Bartonella henselae* infection (Lappin & Black, 1999; Chomel *et al.*, 2003; Ketring *et al.*, 2004; Stiles, 2011).

Treatment

There is no certainty of antimicrobial efficacy for feline bartonellosis treatment, and there is a risk of

continuous re-infection due to absence of immunologic memory to the agent, in case of continuous flea exposure (Kordick *et al.*, 1997; AAFF, 2006).

Treatment is considered to be difficult and should last for at least four to six weeks and often proves to be ineffective, due to bacterial intermittent nature and intracellular characteristic (Holf, 1991; Regnery *et al.*, 1996; Kordick *et al.*, 1997).

In a study, Kordick *et al.* (1997) evaluated doxycycline and enrofloxacin effectiveness in treating cats known to be infected, and reported difficulty in achieving good results by choosing a specific treatment protocol, due to the high bacteremic fluctuation during the natural course of the disease. However, enrofloxacin (3,5-11,4mg/kg, orally, twice a day for 28 days) apparently eliminated bacteremia from five of a total of seven cats. On the other hand, enrofloxacin is contraindicated in doses higher than 5mg/kg, because it may cause retina degeneration and blindness in some cats (Wiebe, 2002). Doxycycline also shows to be effective in treating the disease, when used in 6,9-12,8mg/kg, orally, twice a day for 14 days or 4-10,4mg/kg, orally, twice a day for 28 days.

In the same study, the authors suggest that, due to the risk of developing bacterial resistance, treatment recommendation of the cat should only be considered when the owner is immunocompromised or as an alternative when the animal is at risk of euthanasia.

According to the American Association of Feline Practitioners - AAFF (2006), since there is no report of a proven effective drug to treat cats, some medicines used in humans, such as fluoroquinolones and azithromycin shouldn't be prescribed for bacterial infections in cats if there are other alternatives to treatment. Thus, doxycycline (10mg/kg, orally, twice or once a day) or amoxicillin-clavulanate (22mg/kg, orally, twice a day) should be the first choice medications. Besides treatment, flea control is essential and, since symptomatic animals are probably in bacteremia, additional care such as avoiding bites and scratches should be taken.

BARTONELLOSIS IN HUMANS

Zoonotic importance

Bartonella henselae is known as the main causative agent of Bacillary Angiomatosis, Bacillary Peliosis and cat scratch disease (CSD) in humans. CSD cause classic symptoms of regional lymphadenopathy, fever, malaise, headache and papules that turn into pustules at the inoculation site (Chomel et al., 1995; Kordick & Breitschwerdt, 1995; Breitschwerdt & Kordick, 2000; Guptill et al., 2000; Boulouis et al., 2005).

In most cases, the disease is self-limiting in immunocompetent individuals, however, in immunosuppressed people, such as children or HIV-positive individuals, the disease may have a fatal outcome and antibiotic therapy should be required for a long term. In 5 to 9% of the patients presenting CSD, who face some immunological deficiency, there may be atypical manifestations of disease such as encephalitis, endocarditis, hemolytic anemia, liver and spleen enlargement, glomerulonephritis, pneumonia, intermitent bacteremia, eye injuries, osteomyelitis and a possible change in reproductive performance (Breitschwerdt et al., 2010; Oliveira et al., 2004; Rolain et al., 2004; Chomel et al., 2006).

Transmission to humans

The real importance of the flea as a vector to humans is unknown, but since the presence of fleas is essential for the maintenance of infection in cats, there it is a strong correlation between high flea infestation in cats and high number of cases of the disease identified in humans (Chomel et al., 1996; Breitschwerdt & Kordick, 2000).

The primary mode of transmission is through the contaminated cat nails with flea feces as well as their teeth (Breitschwerdt & Kordick, 2000). However, although there is no scientific evidence, ticks can represent a risk of transmission of *B. henselae* since the agent was detected in *Ixodes ricinus* collected in humans (Sanogo et al., 2003).

In addition, a study in the United States showed the possibility of intrauterine transmission or during the cesarean procedure of *B. henselae* from the mother to her child (Breitschwerdt et al., 2010).

Occurrence in humans in Brazil and in other countries

In Brazil, a study conducted in Piau city, Minas Gerais state, detected seropositivity to *B. henselae* in 60 individuals (13,7%) in a total of 437 (Costa et al., 2005). Another research in Brazil, in Rio de Janeiro

city (Lamas et al., 2010), serologically evaluated HIV-infected individuals and samples from a blood bank. IgG antibodies to *Bartonella* spp. were found in 38,4% of the patients (48/125) and in 34,4% (43/125) of the blood donors. It's a high number since some studies have proven that microorganisms of the *Bartonellae* family are able to survive in blood samples stored for at least 35 days, showing the possible transmission by blood transfusion (Reine, 2004).

Moreover, in the same study (Lamas et al., 2010), 65% (13/20) of the patients who reported ownership of cats in home were seropositives versus 34% (22/65) of those who didn't report animal contact so that the authors found a close relationship among breeding cats and possible infection of *Bartonella* spp.

In a case reported by Breitschwerdt et al. (2011), in the United States, antibodies against *B. koehlerae* as well as the agent itself were detected by PCR test, in a 18 year- old woman who had presented progressive abnormal neurocognitive signs for four years, showing signs of depression, anxiety, headache, muscle spasms, interphalangeal joint stiffness, decreased peripheral vision, decreased tactile sensation and hallucinations. The patient was treated for a long period and there was improvement in clinical status.

Another study in the United States revealed that from 49 patients presenting Bacillary Angiomatosis and/or Bacillary Peliosis, 26 were infected to *B. henselae* and found to be epidemiologically associated to cats or fleas exposure (Koehler et al., 1997).

In a report described by Murinello et al. (2010), in Portugal, a 44 year-old woman was diagnosed with CSD after being scratched by her young and newly acquired cat. The inoculation site had swollen up, with the presence of papules, crusting, pain and regional lymphadenopathy. The diagnosis was confirmed through Indirect Immunofluorescence serologic test and PCR from the biopsy of the axillary node. Also, agent detection was possible by molecular biology from the blood of the patient's cat. It's noteworthy in this context, the importance of tests such as PCR to quick and accurate confirmation of the disease as early as possible.

A study carried out in Rio de Janeiro city described two probable cases and 11 confirmed cases of bacillary angiomatosis, by histopathologic examination, in people presenting Human Immunodeficiency Virus (HIV-1) from five public referral hospitals in treatment of AIDS (Gazineo et

al., 2001). The most frequent clinical signs observed were cutaneous lesions, fever, anorexia, liver enlargement and lymphadenopathy, and a case of Hepatic Bacillary Peliosis was detected in post-mortem examination in one of the patients. Bacillary peliosis is characterized by vascular proliferation lesions in addition to capillary dilatation, formation of cavernous spaces filled with blood in the liver, spleen or bone marrow. Seven patients died due to a probable cause of bacillary angiomatosis.

In a case reported by Velho *et al.* (2006), in Brazil, a woman diagnosed with AIDS presented symptoms suggestive of Bacillary Angiomatosis, such as papular and papulo-nodular lesions, hemorrhagic and pain throughout the body as well as fever and a history of living with multiple cats. The disease was detected by pathological examination, characterized by the authors as an important diagnostic method, especially when serology is not available. The pathological findings were basically atrophic epidermis, dermis with numerous capillaries lined by endothelial edematous cells, cellular atypia, neutrophilic infiltrate and the presence of innumerable bacilli. In addition to the laboratory results, clinical findings and successful therapy with tetracycline were taken together to achieve the definitive diagnosis.

Researchers concluded that we still don't know enough about the real importance of this infection, but it's certain that *Bartonella* are potentially fatal. Thus, further research must be conducted in order to gain more information about the issue (Velho *et al.*, 2006).

In case related by Lamas *et al.* (2007), in Rio de Janeiro city, a man with a history of cardiopathy, was complaining of fatigue and dyspnea after light exercise in the last four months and, by anamnesis, it was found he had been exposed to a young cat a few months before the onset of signs. The histopathology of the excised native aortic valve revealed a vegetative shape suggestive of bacterial endocarditis. Culture of blood and the valve material was performed, as well as molecular biology and Indirect Immunofluorescence Serologic test, in attempt to detect antibodies against *B. henselae*. Despite of the negative results of the culture and PCR test, the diagnosis was established based on the high IgG titer (1:4096) before the beginning of treatment with antibiotics, and a lower titer 14 months after treatment (1:512).

Lamas *et al.* (2007) concluded that the possibility of the occurrence of many endocarditis cases caused by *Bartonella* species exists, but they are not considered

by a great number of doctors. In addition, there is little information from reference laboratories about laboratory diagnostic methods that can be used to help on definitive diagnosis of this agent.

In Brazil, Minas Gerais state, Souza (2011) reported a case of a 79 year-old woman presenting cervical ulcerated adenopathy after close contact with cats. According to the author, the diagnosis was suggestive of CSD after specific findings on histopathology, clinical signs, therapy response and exclusion of other diseases that can cause similar symptoms.

The main laboratory diagnostic methods used for Bartonellosis

Despite of the fact that some authors consider the Indirect Immunofluorescence Serological test as the gold standard for detecting *Bartonella* species infection (Lamas *et al.*, 2008), other researchers report that there is no gold standard method to detect it (AAFP, 2006; Velho *et al.*, 2006). However, the negative culture, PCR and serological results strongly indicate that the animal is not a potential source of transmission of the bacteria to other cats and humans (AAFP, 2006).

In general, the diagnosis can be performed basically through the culture of blood or tissue samples, by detection of specific antibodies in serum, cerebrospinal fluid or aqueous humor and/or by detection of specific DNA fragment through Polymerase Chain Reaction (PCR) from tissue samples and body fluids (AAFP, 2006).

The isolation of *Bartonella* species indicates current infection, however, despite of the greater sensitivity of blood culture versus genetic detection techniques (Zanutto *et al.*, 2001), the main limitations to perform this test are the necessity of specialized laboratories and a long period to obtain the results, since these microorganisms are fastidious, grow slowly and the material can't be dropped off before 56 days, so that it doesn't apply to the routine of most clinical pathology laboratories (Breitschwerdt & Kordick, 2000; Fenollar and Raoult, 2004; AAFP, 2006; Velho *et al.*, 2006).

The serological tests such as ELISA and Indirect Immunofluorescence have been widely used for the diagnosis of *Bartonella* species because they are fast and affordable. However, positive results are not able to distinguish between current infection or simple exposure to the agent, and they can't

differentiate the infecting species. In addition, negative results don't rule out infection (AAFP, 2006; Velho *et al.*, 2006). Moreover, serological tests may be limited by the possibility of cross-reactivity among different species of bacteria as well as other agents like *Coxiella* and *Chlamydia* (La Scola & Raoult, 1996; Maurin *et al.*, 1997; Costa *et al.*, 2005).

PCR requires specialized laboratories and its performance can be expensive, but the results are obtained faster than by culture and isolation and allow the discrimination among species, in opposite to serological tests. For these reasons, PCR is recommended in order to diagnose exposure to the agent and infection of cats with *Bartonella* spp. (Fenollar & Raoult, 2004; AAFP, 2006; Souza *et al.*, 2010).

According to the AAFP (2006), diagnosis can be achieved when there are consistent and reported clinical signs related to feline Bartonellosis in addition to the exclusion of other diseases that show similar clinical signs, a positive laboratory test (culture, PCR or serology) and therapy response when recommended drugs are used.

However, even when these criteria are met, due to tests limitations and the wide spectrum efficacy achieved with recommended treatments, which may mess up the diagnosis of other diseases with similar symptomatology, doctors may face difficulties in obtaining the definitive diagnosis (AAFP, 2006).

FINAL CONSIDERATIONS

Thus, as higher prevalences of the disease are found in tropical countries (Boulouis *et al.*, 2005), further studies are mandatory in Brazil in order to adopt prevention and control measures.

Besides, studies in order to confirm *Bartonella* spp. infections in pet cats are extremely important, considering that these are important zoonotic and occupational diseases, mainly in immunocompromised people and Veterinarians.

Once diagnosis and treatment of the disease in cats are complex and there is no vaccine available, it is essential that vector control measures are adopted, by periodically using effective flea control strategies. Cats must not receive blood transfusions from an unknown cat or from those that are known to be infected with *Bartonella* spp. In addition, bites

and scratches must be avoided, especially by immunocompromised people and professionals who deal directly with cats.

REFERÊNCIAS

AAFP - Association of Feline Practitioners. 2006. Panel report on diagnosis, treatment, and prevention of *Bartonella* species infections. Journal of Feline Medicine and Surgery. 8:213-226.

ABBOTT, R.C., CHOMEL, B.B., KASTEN, R.W., FLOYDHAWKINS, K.A., KIKUCHI, Y., KOEHLER, J.E. & PEDERSEN, N.C. 1997. Experimental and natural infection with *Bartonella henselae* in cats. Comparative Immunology Microbiology and Infectious Disease. 20(1):41-57.

BOULOUIS, H.J., CHANG, C., HENN, J.B., KASTEN, R.W. & CHOMEL, B.B. 2005. Factors associated with the rapid emergence of zoonotic *Bartonella* infections. Veterinary Research. 36:383-410.

BORTOLI, C.P.; ANDRÉ, M.R.; SEKI, M.C.; PINTO, A.A.; MACHADO, S.T.Z.; MACHADO, R.Z. Detection of hemoplasma and *Bartonella* species and co-infection with retroviruses in cats subjected to a spaying/neutering program in Jaboticabal, SP, Brazil. Revista Brasileira de Parasitologia Veterinária. 21(3):219-223.

BRAGA, M.S.C.O.; DINIZ, P.P.V.P.; ANDRÉ, M.R.; BORTOLI, C.P.; MACHADO, R.Z. 2012. Molecular characterisation of *Bartonella* species in cats from São Luís, state of Maranhão, north-eastern Brazil. Memórias do Instituto Oswaldo Cruz. 107(6):772-777.

BREITSCHWERDT, E.B. & KORDICK, D.L. 2000. *Bartonella* infection in animals: carriership, reservoir potential, pathogenicity, and zoonotic potential for human infection. Clinical Microbiology Reviews. 13:428-438.

BREITSCHWERDT, E.B. 2008. Feline bartonellosis and cat scratch disease. Veterinary Immunology and Immunopathology. 15:167-171.

BREITSCHWERDT, E.B., MAGGI, R.G., FARMER, P. & MASCARELLI, P.E. 2010. Molecular Evidence of Perinatal Transmission of *Bartonella vinsonii* subsp. *berkhoffii* and *Bartonella henselae* to a Child. Journal of Clinical Microbiology. 48(6):2289-2293.

BREITSCHWERDT, E.B., MASCARELLI, P.E., SCHWEICKERT, L.A., MAGGI, R.G., HEGARTY, B.C., BRADLEY, J.M. & WOODS, C.W. 2011. Hallucinations, Sensory Neuropathy, and Peripheral Visual Deficits in a Young Woman Infected with *Bartonella koehlerae*. Journal of Clinical Microbiology. 49(9):3415-3417.

- BRENNER, D.J., O'CONNOR, S.P., WINKLER, H.H. & STEIGERWALT, A.G. 1993. Proposals to Unify the Genera *Bartonella* and *Rochalimaea*, with Descriptions of *Bartonella quintana* comb. nov., *Bartonella vinsonii* comb. nov., *Bartonella henselae* comb. nov. and *Bartonella elizabethae* comb. nov. and to Remove the Family *Bartonellaceae* from the Order *Rickettsiales*. International Journal of Systematic Bacteriology. 43(4):777-786.
- CHOMEL, B.B., ABBOTT, R.C., KASTEN, R.W., FLOYD-HAWKINS, K.A., KASS, P.H., GLASER, C.A., PEDERSEN, N.C. & KOEHLER, J.E. 1995. *Bartonella henselae* prevalence in domestic cats in California: risk factors and association between bacteremia and antibody titers. Journal of Clinical Microbiology. 33:2445-2450.
- CHOMEL, B.B., KASTEN, R.W., FLOYD-HAWKINS, K., CHI, B., YAMAMOTO, K., ROBERTS-WILSON, J., GURFIELD, A.N., ABBOTT, R.C., PEDERSEN, N.C. & KOEHLER, J.E. 1996. Experimental transmission of *Bartonella henselae* by the cat flea. Journal of Clinical Microbiology. 34:1952-1956.
- CHOMEL, B.B., WEY, A.C., KASTEN, R.W., STACY, B.A. & LABELLE, P. 2003. Fatal Case of Endocarditis Associated with *Bartonella henselae* Type Infection in a Domestic Cat. Journal of Clinical Microbiology. 41(11):5337-5339.
- CHOMEL, B.B., BOULOUIS, H.J. & BREITSCHWERDTE, B. 2004. Cat scratch disease and other zoonotic *Bartonella* infections. Journal of the American Veterinary Medical Association. 224 (8):1270-1279.
- CHOMEL, B.B., BOULOUIS, H.J., MARUYAMA, S. & MOLIA, S. 2006. *Bartonella* spp. in pets and effect on human health. Emerging Infectious Diseases. 12(3):389-394.
- CHUNG, C.Y., KASTEN, R.W., PAFF, S.M., VAN HORN, B.A., VAYSSIER-TAUSSAT, M., BOULOUIS, H.J. & CHOMEL, B.B. 2004. *Bartonella* spp. DNA associated with biting flies from California. Emerging Infectious Diseases. 10(7):1311-1313.
- COSTA, P.S.G., BRIGATTE, M.E. & GRECO, D.B. 2005. Antibodies to *Rickettsia rickettsii*, *Rickettsia typhi*, *Coxiella burnetii*, *Bartonella henselae*, *Bartonella quintana*, and *Ehrlichia chaffeensis* among healthy population in Minas Gerais, Brazil. Memórias do Instituto Oswaldo Cruz. 100(8):853-859.
- CRISSIUMA, A., FAVACHO, A., GERSHONY, L., ALMEIDA, F.M., GOMES, R., MARES-GUIA, A., ROZENTAL, T., BARREIRA, J., LEMOS, E. & LABARTHE, N. 2011. Prevalence of *Bartonella* species DNA and antibodies in cats (*Felis catus*) submitted to a spay/neuter program in Rio de Janeiro, Brazil. Short communication, Journal of Feline Medicine and Surgery. 13:149-151.
- DOWERS, K.L., HAWLEY, J.R., BREWER, M.M., MORRIS, A.K., RADECKI, S.V. & LAPPIN, M.R. 2010. Association of *Bartonella* species, feline calicivirus, and feline herpesvirus 1 infection with gingivostomatitis in cats. Journal of Feline Medicine and Surgery. 12(4):314-321.
- FENOLLAR, F. & RAOULT, D. 2004. Molecular genetic methods for the diagnosis of fastidious microorganisms. Acta Pathologica, Microbiologica et Immunologica Scandinavica. 112: 785-807.
- FOIL, L., ANDRESS, E., FREELAND, R.L., ROY, A.F., RUTLEDGE, R., TRICHE, P.C.; O'REILLY, K.L. 1998. Experimental infection of domestic cats with *Bartonella henselae* by inoculation of *Ctenocephalides felis* (Siphonaptera: Pulicidae) feces. Journal of Medical Entomology. 35:625-628.
- GAZINEO, J.L.D., TROPE, B.M., MACEIRA, J.P., MAY, S.B., COELHO, J.M.C.O., LAMBERT, J.S. & NOGUEIRA, S.A. 2001. Bacillary angiomatosis: description of 13 cases reported in five reference centers for aids treatment in Rio de Janeiro, Brazil. Revista do Instituto de Medicina Tropical de São Paulo. 43(1):1-6.
- GUPTILL, L., SLATER, L., WU, C.-C., LIN, T.L., GLICKMAN, L.T., WELCH, D.F. & HOGENESCH, H. 1997. Experimental infection of young specific pathogen-free cats with *Bartonella henselae*. Journal of Infectious Disease. 176:206-216.
- GUPTILL, L., SLATER, L., WU, C.-C., LIN, T.L., GLICKMAN, L.T., WELCH, D.F., TOBOLSKI, J. & HOGENESCH, H. 1998. Evidence of reproductive failure and lack of perinatal transmission of *Bartonella henselae* in experimentally infected cats. Veterinary Immunology and Immunopathology. 65:177-189.
- GUPTILL, L., WU, C.C., GLICKMAN, L., TUREK, J., SLATER, L. & HOGENESCH, H. 2000. Extracellular *Bartonella henselae* and artifactual intraerythrocytic pseudoinclusions in experimentally infected cats. Veterinary Microbiology. 76:283-290.
- GUPTILL, L., WU, C.-C., HOGENESCH, H., SLATER, L.N., GLICKMAN, N., DUNHAM, A., SYME, H. & GLICKMAN, L. 2004. Prevalence, risk factors, and genetic diversity of *Bartonella henselae* infections in pet cats in four regions of the United States. Journal of Clinical Microbiology. 42(2):652-659.
- GUPTILL, L. 2010. Bartonellosis. Veterinary Microbiology. 140:347-359.
- HELLER, R., ARTOIS, M., XEMAR, V., BRIEL, D., GEHIN, H., JAULHAC, B., MONTEIL, H. & PIEMONT, Y. 1997. Prevalence of *Bartonella henselae* and *Bartonella clarridgeiae* in Stray Cats. Journal of Clinical Microbiology. 35(6):1327-1331.

- HOLF, H. 1991. Intracellular microorganisms: A particular problem for chemotherapy. *Infection*. 19(4):193-194.
- KETRING, K.L., ZUCKERMAN, E.E., & HARDY, W.D. 2004. *Bartonella*: a new etiological agent of feline ocular disease. *Journal of the American Animal Hospital Association*. 40:6-12.
- KIKUCHI, E., MARUYAMA, S., SAKAI, T., TANAKA, S., YAMAGUCHI, F., HAGIWARA, T., KATSUBE, Y., MIKAMI, T. 2002. Serological investigation of *Bartonella henselae* infections in clinically cat-scratch disease-suspected patients, patients with cardiovascular diseases, and healthy veterinary students in Japan. *Microbiology and Immunology*. 46:313-316.
- KOEHLER, J.E., SANCHEZ, M.A. & GARRIDO, C.S. 1997. Molecular epidemiology of *Bartonella* infections in patients with bacillary angiomatosis-peliosis. *The new England Journal of Medicine*. 337(26):1876-1883.
- KORDICK, D.L. & BREITSCHWERDT, E.B. 1995. Intraerythrocytic presence of *Bartonella henselae*. *Journal of Clinical Microbiology*. 33:1655-1656.
- KORDICK, D.L., PAPICH, M.G., & BREITSCHWERDT, E.B. 1997. Efficacy of Enrofloxacin or Doxycycline for Treatment of *Bartonella henselae* or *Bartonella clarridgeiae* Infection in Cats. *Antimicrobial Agents and Chemotherapy*. 41(11):2448-2455.
- KORDICK, D.L., BROWN, T.T., SHIN, K. & BREITSCHWERDT, B. 1999. Clinical and pathologic evaluation of chronic *Bartonella henselae* or *Bartonella clarridgeiae* infection in cats. *Journal of Clinical Microbiology*. 37:1536-1547.
- LA SCOLA, B. & RAOULT, D. 1996. Serological cross-reactions between *Bartonella quintana*, *Bartonella henselae* and *Coxiella burnetii*. *Journal of Clinical Microbiology*. 34(9):2270-2274.
- LAMAS, C.; FAVACHO, A.; RAMOS, R.G., SANTOS, M.S., FERRAVOLI, G.I., WEKSLER, C., ROZENTAL, T., BÓIA, M.N. & LEMOS, E.R.S. 2007. *Bartonella* native valve endocarditis: The First Brazilian Case Alive and Well. *The Brazilian Journal of Infectious Disease*. 11(6):591-594.
- LAMAS, C.; CURI, A.; BÓIA, M.N. & LEMOS, E.R.S. 2008. Human bartonellosis: seroepidemiological and clinical features with an emphasis on data from Brazil- A Review. *Memórias do Instituto Oswaldo Cruz*. 103(3):221-235.
- LAMAS, C.C., MARES-GUIA, M.A., ROZENTAL, T., MOREIRA, N., FAVACHO, A.R.M., BARREIRA, J., GUTERRES, A., BÓIA, M.M. & LEMOS, E.R.S. 2010. *Bartonella* spp. infection in HIV positive individuals, their pets and ectoparasites in Rio de Janeiro, Brazil: Serological and molecular study. *Acta Tropica*. 115:137-141.
- LAPPIN, M.R. & BLACK, J.C. 1999. *Bartonella* spp. Infection as a possible cause of uveitis in a cat. *Journal of the American Veterinary Medical Association*. 214(8):1205-1207.
- MAGALHÃES, R.F., PITASSI, L.H.U., SALVADEGO, M., MORAES, A.M., BARJAS-CASTRO, M.L., VELHO, P.E.N.F. 2008. *Bartonella henselae* survives after the storage period of red blood cell units: is it transmissible by transfusion? *Transfusion Medicine*. 18(5):287-291.
- MAURIN, M., ETIENNE, J. & RAOULT, D. 1997. Serological cross-reactions between *Bartonella* and *Chlamydia* species: implications for diagnosis. *Journal of Clinical Microbiology*. 35(9): 2283-2287.
- MOGOLLON-PASAPERA, E., OTVOS JR, L. & GIORDANO, A. 2009. *Bartonella*: emerging pathogen or emerging awareness? *International Journal of Infectious Disease*. 13:3-8.
- MURINELLO, N., MURINELLO, A., DAMÁSIO, H., CARVALHO, A. & SOUSA, R. 2010. Cat-Scratch disease in a 44-year-old woman. *Revista Portuguesa de Doenças Infecciosas*. 6(3):112-118.
- OLIVEIRA, A.H.P., PEREIRA, C.A.P., SOUZA, L.B. & FREITAS, D. 2004. Conjuntivite granulomatosa atípica causada pela doença da arranhadura do gato- Relato de caso. *Arquivos Brasileiros de Oftalmologia*. 67:541-543.
- PONS, I., SANFELIU, I., QUESADA, M., ANTON, E., SAMPERE, M., FONT, B., PLA, J. & SEGURA, F. 2005. Prevalence of *Bartonella henselae* in cats in Catalonia, Spain. *The American Journal of Tropical Medicine and Hygiene*. 72(4):453-457.
- QUIMBY, J.M., ELSTON, T., HAWLEY, J., BREWER, M., MILLER, A. & LAPPIN, M.R. 2008. Evaluation of the association of *Bartonella* species, feline herpesvirus 1, feline calicivirus, feline leukemia virus and feline immunodeficiency virus with chronic feline gingivostomatitis. *Journal of Feline Medicine and Surgery*. 10:66-72.
- REGNERY, R.L., ANDERSON, B.E., CLARRIDGE, J.E., RODRIGUEZ-BARRADAS, M.C., JONES, D.C. & CARR, J.H. 1992a. Characterization of a Novel *Rochalimaea* Species, *R. henselae* sp. nov., Isolated from Blood of a Febrile, Human Immunodeficiency Virus-Positive Patient. *Journal of Clinical Microbiology*. 30(2):265-274.
- REGNERY, R., MARTIN, M. & OLSON, J. 1992b. Naturally occurring “*Rochalimaea henselae*” infection in domestic cat. *Lancet*. 340(8818):557-558.
- REGNERY, R.L., ROONEY, J.A., JOHNSON, A.M., NESBY, S.L., MANZEWITSCH, P., BEAVER, K. &

OLSON, J.G. 1996. Experimentally induced *Bartonella henselae* infections followed by challenge exposure and antimicrobial therapy in cats. American Journal of Veterinary Research. 57(12):1714-1719.

REINE, N. J. 2004. Infection and blood transfusion: a guide to donor screening. Clinical Techniques in Small Animal Paractice. 19(2):68-74.

ROLAIN, J.M., BROUQUI, P., KOEHLER, J.E., MAGUINA, C., DOLAN, M.J. & RAOULT, D. 2004. Recommendations for treatment of human infections caused by *Bartonella* species. Antimicrobial Agents and Chemotherapy. (48):1921-1933.

SANOGO, Y.O., ZEAITER, Z., CARUSO, G., MEROLA, F., SHPYNOV, S., BROUQUI, P. & RAOULT, D. 2003. *Bartonella henselae* in *Ixodes ricinus* ticks (Acari: Ixodida) removed from humans, Belluno Province, Italy. Emerging Infectious Diseases. 9(3):329-332.

SOUZA, A.M., ALMEIDA, D.N.P., GUTERRES, A., GOMES, R., FAVACHO, A.R.M., MOREIRA, N.S., MAIA, L.M.P., ROZENTAL, T., FILHO, R.A.T., CERQUEIRA, A.M.F., LEMOS, E.R.S. & ALMOSNY, N.R.P. 2010. Bartonelose: análise molecular e sorológica em gatos do Rio de Janeiro – Brasil. Revista Brasileira de Ciência Veterinária. 27(1):7-11.

SOUZA, G.F. 2011. Doença da arranhadura do gato: relato de caso. Revista Médica de Minas Gerais. 21(11):75-78.

STAGGEMEIR, R., VENKER, C.A., KLEIN, D.H., PETRI, M., SPILKI, F.R. & CANTARELLI, V.V. 2010. Prevalence of *Bartonella henselae* and *Bartonella clarridgeiae* in cats in the south of Brazil: a molecular study. Memórias do Instituto Oswaldo Cruz. 105(7):873-878.

STILES, J. 2011. Bartonellosis in cats: a role in uveitis? Veterinary Ophthalmology. 14(1):9-14.

VELHO, P.E.N.F., MORAES, A.M., SOUZA, E.M., UTHIDA-TANAKA, A.M. & CINTRA, M.L. 2006. Diagnóstico da infecção por *Bartonella* spp.: a propósito de um caso de angiomatose bacilar. Anais Brasileiros de Dermatologia. 81(4):349-353.

WIEBE, V. 2002. Fluoroquinolone-induced retinal degeneration in cats. Journal of the American Veterinary Medical Association. 221(11):1568-1571.

ZANUTTO, M.S., MAMIZUCA, E.M., JÚNIOR, R.R., LIMA, T.M., DIOGO, C.L., OKAY, T.S. & HAGIWARA, M.K. 2001. Experimental infection and horizontal transmission of *Bartonella henselae* in domestic cats. Revista do Instituto de Medicina Tropical de São Paulo. 43(5):257-261.