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Cat scratch disease: Current advances in *Bartonella henselae* infection from a one health perspective - A review

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Abstract
Cat scratch disease (CSD) is an important zoonotic infection caused primarily by *Bartonella henselae*, a fastidious intracellular Gram-negative bacterium maintained in domestic cats, with transmission largely sustained by the cat flea (*Ctenocephalides felis*). Once considered a mild illness limited to regional lymphadenopathy after a cat scratch or bite, CSD is now recognized as a clinically diverse disease capable of affecting multiple organ systems. In addition to its classical presentation, *B. henselae* infection has been associated with ocular disease, neurobartonellosis, hepatosplenic involvement, osteomyelitis, infective endocarditis and bacillary angiomatosis, particularly in immunocompromised individuals. Recent advances in molecular diagnostic techniques have greatly improved the detection of *Bartonella* infections and have expanded current understanding of bacterial diversity, host adaptation, and transmission dynamics. Domestic cats remain the principal reservoir, while flea infestation plays a central role in maintaining infection within feline populations and facilitating indirect transmission to humans. The increasing global population of companion animals, together with changing environmental and vector-related factors, has renewed interest in CSD as a significant One Health concern. This review summarizes current knowledge on the epidemiology, pathogenesis, clinical manifestations, diagnosis, treatment, and prevention of cat scratch disease, with emphasis on recent developments in molecular epidemiology and host–pathogen interactions. It also highlights the importance of coordinated efforts involving physicians, veterinarians, microbiologists, and public health professionals to improve surveillance, promote responsible pet ownership and flea control, and strengthen integrated One Health strategies for reducing the impact of this increasingly recognized zoonotic disease.

Keywords: *Bartonella henselae*, cat scratch disease, zoonosis, One Health, companion animals, flea-borne infection, public health

Introduction
The growing bond between humans and companion animals has brought undeniable social and health benefits, but it has also increased opportunities for the transmission of zoonotic pathogens. Among bacterial zoonoses associated with cats, cat scratch disease (CSD) remains one of the most common yet frequently underrecognized infections affecting humans. The disease is caused predominantly by *Bartonella henselae*, a fastidious Gram-negative intracellular bacterium that has evolved remarkable adaptations for persistent infection in its feline reservoir while retaining the capacity to infect humans (Chomel *et al.,* 2006; Harms and Dehio, 2012) [7, 12]. For many years, CSD was regarded as a mild, self-limiting illness, particularly in children, with regional lymphadenopathy developing after a cat scratch or bite. This traditional view has changed considerably. Clinical and molecular studies over the past two decades have shown that *B. henselae* infection extends well beyond localized lymph node disease. Ocular disorders, neurological complications, hepatosplenic involvement, osteomyelitis, infective endocarditis, and other systemic manifestations are now increasingly recognized, highlighting the broad clinical spectrum of this infection (Florin *et al.,* 2008; Breitschwerdt *et al.,* 2024) [6, 9]. These findings indicate that Bartonella infections are more complex than previously appreciated and remain an important diagnostic consideration in patients with compatible clinical histories. Parallel advances in molecular biology have transformed the understanding of Bartonella infections. The introduction of polymerase chain reaction (PCR), multilocus sequence typing, and next-generation sequencing has greatly improved the detection and characterization of *Bartonella* species, revealing greater genetic diversity, refining knowledge of transmission pathways, and providing new insights into bacterial evolution and host–pathogen interactions (McCormick *et al.,* 2023). These developments have not only enhanced diagnostic accuracy but have also stimulated renewed interest in Bartonella as an emerging pathogen of both medical and veterinary importance.
Cat scratch disease exemplifies the interconnected nature of human, animal, and environmental health. Domestic cats serve as the principal reservoir, flea vectors sustain transmission within feline populations, and human infection is closely linked to interactions among animals, vectors, and their shared environment. This close relationship places CSD firmly within the framework of the One Health

concept, emphasizing the need for collaboration among physicians, veterinarians, microbiologists, entomologists, and public health professionals. Accordingly, this review summarizes current knowledge on the epidemiology, transmission, pathogenesis, clinical manifestations, diagnosis, treatment, and prevention of cat scratch disease while identifying emerging research priorities and knowledge gaps relevant to both human and veterinary medicine.

Epidemiology and Ecology

Cat scratch disease (CSD) has a global distribution and occurs wherever domestic cats and their primary ectoparasite, the cat flea (*Ctenocephalides felis*), are present. Although cases have been reported from every inhabited continent, the epidemiology of the disease differs considerably across geographic regions. Climatic conditions, flea abundance, cat population density, animal management practices, and patterns of human–animal interaction collectively influence the prevalence and transmission dynamics of *Bartonella henselae* infection (Guptill, 2010) [11].

Domestic cats are the principal reservoir host of *B. henselae*, often harboring persistent bacteremia without showing obvious clinical signs. Serological and molecular investigations have demonstrated marked geographic variation in feline infection rates, with reported prevalences ranging from less than 5% in temperate regions to more than 50% in tropical and subtropical areas (Chomel *et al.,* 2006) [7]. These differences are largely attributed to variations in flea infestation, as the cat flea is essential for maintaining bacterial circulation within feline populations. Environmental conditions that favor flea survival therefore play a pivotal role in sustaining the natural transmission cycle of the pathogen.

Age is another important epidemiological determinant. Young cats, particularly kittens, are more frequently bacteremic than adult animals and are considered the most efficient source of human infection. Their greater likelihood of flea infestation, coupled with playful behavior that often results in scratches or bites, increases the risk of bacterial transmission. Consequently, close contact with kittens has consistently been identified as one of the strongest risk factors for developing CSD in humans (Nelson *et al.,* 2016).

Seasonal trends have also been observed in several epidemiological studies. In France, Angelakis *et al*. (2011) documented a marked increase in CSD cases during autumn and winter. Comparable seasonal patterns reported from other countries are thought to reflect fluctuations in flea populations, increased indoor housing of companion animals during colder months, and more frequent close contact between cats and their owners.

Despite its worldwide occurrence, the true burden of CSD remains difficult to estimate. Many infections are mild, self-limiting, and never reach medical attention, while limited surveillance systems and inconsistent use of laboratory confirmation contribute to substantial underreporting. In the United States alone, an estimated 12,000 outpatient consultations and approximately 500 hospitalizations are attributed to CSD each year (Nelson *et al.,* 2016). However, these figures likely represent only a fraction of the actual number of infections, underscoring the need for improved surveillance, standardized reporting systems, and broader application of sensitive diagnostic methods to better define the global epidemiology of this emerging zoonosis.

Pathogenesis and Host–Pathogen Interactions

The pathogenic success of *Bartonella henselae* lies in its remarkable ability to establish long-lasting infection while avoiding elimination by the host immune system. Unlike many bacterial pathogens that produce acute, self-limiting infections, *Bartonella* species have evolved highly specialized mechanisms that enable prolonged persistence within their mammalian hosts with minimal inflammatory damage. This unique host–pathogen relationship facilitates chronic bacteremia in reservoir animals and creates repeated opportunities for zoonotic transmission.

Human infection is usually initiated when *B. henselae*-contaminated flea feces are introduced into the skin through a cat scratch, bite, or other minor skin injury. After entering the host, the organism initially colonizes the dermis and regional lymphatic tissues before disseminating via the bloodstream. A defining characteristic of *B. henselae* infection is its ability to invade and survive within erythrocytes and vascular endothelial cells, where the bacterium is relatively protected from circulating antibodies and other humoral immune defenses (Harms and Dehio, 2012) [12]. This intracellular niche not only promotes bacterial persistence but also contributes to the prolonged bacteremia commonly observed in infected cats.

Successful colonization depends on a sophisticated repertoire of bacterial virulence factors that manipulate host cellular functions. Among these, Bartonella adhesin A (BadA) plays a crucial role by mediating firm attachment to endothelial cells and extracellular matrix proteins. In addition, the type IV secretion system (T4SS) translocates a range of effector proteins directly into host cells, altering intracellular signaling pathways to suppress apoptosis, modulate inflammatory responses, and create a cellular environment favorable for bacterial survival and replication (Barbour *et al.,* 2023). These molecular interactions allow the organism to evade immune clearance while maintaining long-term infection.

One of the most distinctive features of *B. henselae* pathogenesis is its ability to stimulate abnormal vascular proliferation. Experimental studies have shown that infection induces the expression of vascular endothelial growth factor (VEGF) and several other pro-angiogenic mediators, leading to excessive endothelial cell proliferation. This angiogenic response underlies the development of bacillary angiomatosis and peliosis hepatis, two characteristic manifestations seen predominantly in immunocompromised patients. The capacity to induce pathological angiogenesis distinguishes *B. henselae* from many other bacterial pathogens and contributes significantly to the severity of disseminated disease.

Equally important is the organism's ability to evade both innate and adaptive immune responses. *Bartonella* species exhibit multiple immune-evasion strategies, including resistance to complement-mediated killing, antigenic variation of surface proteins, and modulation of cytokine signaling pathways. These adaptations reduce immune recognition, facilitate intracellular persistence, and help explain the chronic bacteremia observed in cats as well as the prolonged or atypical clinical manifestations occasionally encountered in humans. Collectively, these host–pathogen interactions illustrate the highly adapted

biology of *B. henselae* and provide the mechanistic basis for its persistence, diverse clinical presentations, and continued emergence as a significant zoonotic pathogen.

The clinical spectrum of cat scratch disease (CSD) is considerably broader than previously recognized and ranges from a mild, self-limiting illness to severe multisystem disease. Clinical outcome is influenced by several factors, including bacterial virulence, inoculum size, host immune status, and tissue tropism. Although regional lymphadenitis remains the hallmark of infection, *Bartonella henselae* is capable of involving virtually every organ system, resulting in a wide variety of clinical presentations (Florin *et al.,* 2008; Breitschwerdt *et al.,* 2024) [6, 9].

In its classical form, CSD usually follows a scratch or bite from an infected cat. A small erythematous papule, pustule, or vesicle commonly develops at the site of inoculation within 3–10 days, although this lesion often resolves spontaneously and may pass unnoticed. One to three weeks later, regional lymphadenopathy becomes evident and represents the most characteristic feature of the disease. The affected lymph nodes are typically enlarged, tender, and freely movable, with the axillary, cervical, epitrochlear, and inguinal nodes most frequently involved, depending on the site of inoculation. Many patients also experience mild systemic signs such as low-grade fever, malaise, fatigue, anorexia, and headache, which usually resolve without long-term sequelae (Florin *et al.,* 2008) [9].

While most patients recover uneventfully, approximately 5–15% develop atypical manifestations that extend beyond the lymphatic system. Improved clinical awareness and advances in diagnostic techniques have contributed to increasing recognition of these fewer common presentations. Among them, ocular involvement is one of the best-characterized complications. Parinaud oculoglandular syndrome, characterized by unilateral granulomatous conjunctivitis associated with ipsilateral preauricular lymphadenopathy, is highly suggestive of *Bartonella* infection. Another important ocular manifestation is neuroretinitis, which typically presents with acute visual impairment, optic disc edema, and the classic macular star pattern. *B. henselae* is now regarded as one of the leading infectious causes of neuroretinitis worldwide (Solley *et al.,* 1999; Florin *et al.,* 2008) [9, 17].

Neurological disease, once considered uncommon, is increasingly recognized as an important manifestation of *Bartonella* infection. Recent evidence suggests that neurobartonellosis may be substantially underdiagnosed because of its diverse and often nonspecific clinical presentation (Breitschwerdt *et al.,* 2024) [6]. Patients may present with persistent headache, cognitive dysfunction, encephalopathy, encephalitis, seizures, transverse myelitis, cranial neuropathies, or neuropsychiatric disturbances. Although the exact pathogenic mechanisms remain incompletely understood, endothelial cell invasion, microvascular injury, immune-mediated inflammation, and possible infection of glial cells are thought to contribute to neurological involvement (Barbour *et al.,* 2023).

Visceral disease represents another important but frequently overlooked manifestation of CSD. Hepatosplenic bartonellosis is most often encountered in children and immunocompromised individuals and typically presents as prolonged fever of unknown origin accompanied by abdominal pain, weight loss, and elevated inflammatory markers. Radiological investigations frequently demonstrate multiple hepatic and splenic granulomas or microabscesses. Because these findings may closely resemble tuberculosis, lymphoma, metastatic disease, or systemic fungal infections, diagnosis is often delayed unless Bartonella infection is specifically considered (Spach *et al.,* 1995) [18].

Among the most serious complications of *B. henselae* infection is culture-negative infective endocarditis. Bartonella species have emerged as important causes of blood culture-negative endocarditis, particularly in patients with underlying valvular heart disease or prosthetic valves (Angelakis and Raoult, 2014) [2]. Owing to the fastidious nature of the organism, routine blood cultures are frequently negative, making serological assays and molecular diagnostic techniques essential for establishing the diagnosis. Failure to recognize Bartonella endocarditis promptly may result in progressive valvular destruction, congestive heart failure, and significant mortality.

The clinical picture differs markedly in immunocompromised individuals, especially those with advanced HIV infection, in whom disseminated disease is more common. Bacillary angiomatosis is characterized by proliferative vascular lesions involving the skin, mucous membranes, and internal organs and represents one of the most distinctive manifestations of Bartonella infection. Histopathologically, these lesions exhibit marked angiogenesis driven by bacterial stimulation of vascular growth factors. Peliosis hepatis, characterized by blood-filled cystic cavities within the hepatic parenchyma, is another severe manifestation that may lead to life-threatening complications if left untreated (Koehler *et al.,* 1992) [13].

The expanding spectrum of clinical manifestations has fundamentally changed the understanding of cat scratch disease. Rather than a simple cause of regional lymphadenitis, *B. henselae* is now recognized as a versatile zoonotic pathogen capable of producing localized, disseminated, and organ-specific disease. Awareness of these diverse presentations is essential for timely diagnosis, appropriate treatment, and prevention of potentially serious complications, particularly in individuals at increased risk of severe infection.

The diagnosis of cat scratch disease (CSD) can be challenging because its clinical manifestations range from uncomplicated regional lymphadenitis to multisystem involvement that mimics numerous infectious, inflammatory, and neoplastic disorders. No single laboratory test is sufficiently sensitive or specific to confirm all cases; therefore, diagnosis relies on a combination of epidemiological information, clinical findings, laboratory investigations, and, when required, molecular and histopathological evidence.

A detailed exposure history remains the cornerstone of clinical evaluation. Recent contact with cats, particularly kittens or flea-infested animals, together with a history of scratches, bites, or close handling, substantially increases the likelihood of *Bartonella henselae* infection. Nevertheless, the absence of a recognized scratch should not exclude the diagnosis, as many patients are unable to recall minor injuries or may acquire infection through indirect contamination of broken skin with flea feces.

Serological testing continues to be the most widely available laboratory method for diagnosing CSD. Indirect immunofluorescence assay (IFA) is generally regarded as the reference serological technique, while enzyme-linked

immunosorbent assay (ELISA) is also widely used for detecting *Bartonella*-specific antibodies. Reported sensitivities range from approximately 50% to 95%, reflecting differences in assay methodology, antigen preparation, and patient populations (Vermeulen *et al.,* 2007) [19]. Although serology provides valuable supportive evidence, interpretation should be undertaken with caution because antibody responses may persist after previous exposure and cross-reactivity with organisms such as *Coxiella burnetii* and *Chlamydia* species can reduce diagnostic specificity.

The introduction of molecular diagnostic techniques has markedly improved the identification of *Bartonella* infections, particularly in patients with atypical or disseminated disease. Polymerase chain reaction (PCR) assays targeting conserved genes, including 16S rRNA, gltA, ribC, and ftsZ, provide highly specific detection of *Bartonella* DNA in clinical specimens (McCormick *et al.,* 2023) [14]. Molecular testing is especially valuable in cases of neurobartonellosis, hepatosplenic disease, culture-negative infective endocarditis, and other systemic manifestations where conventional methods often yield inconclusive results. Because bacteremia in humans is typically transient and of low magnitude, tissue specimens obtained from lymph nodes, cardiac valves, or other affected organs generally provide higher diagnostic yields than peripheral blood samples.

Histopathological examination continues to play an important complementary role, particularly when lymph node biopsy is performed to exclude malignancy or other granulomatous diseases. Typical findings include necrotizing granulomatous inflammation with central microabscess formation. Although Warthin–Starry silver staining may demonstrate bacillary organisms within tissue sections, its sensitivity is inconsistent and a negative result does not exclude infection. In recent years, next-generation sequencing and metagenomic diagnostic platforms have emerged as promising technologies for identifying *Bartonella* species directly from clinical specimens, especially in diagnostically challenging cases where conventional microbiological methods fail to establish an etiological diagnosis.

Despite substantial advances in laboratory diagnostics, important challenges remain. Variability among serological assays, the intermittent nature of bacteremia, differences in specimen quality, and the limited availability of advanced molecular techniques continue to affect diagnostic accuracy. Consequently, the most reliable diagnosis is achieved through an integrated approach that combines clinical suspicion with appropriate laboratory investigations, allowing timely recognition of both classical and atypical presentations of cat scratch disease.

Therapeutic Management

The management of cat scratch disease (CSD) should be guided by the severity of illness, extent of organ involvement and the patient's immune status. While the disease is often self-limiting in immunocompetent individuals, antimicrobial therapy plays an important role in selected patients by shortening the duration of symptoms, preventing disease progression, and reducing the risk of serious complications. Consequently, treatment decisions should be individualized rather than based solely on the presence of *Bartonella henselae* infection.

Most patients with uncomplicated CSD present with localized lymphadenitis and mild constitutional symptoms. In these cases, supportive measures such as analgesics, antipyretics, and observation are frequently sufficient, as spontaneous resolution is common. Nevertheless, antimicrobial therapy may hasten clinical recovery. A randomized, placebo-controlled clinical trial demonstrated that azithromycin significantly accelerated the reduction in lymph node size, supporting its use as the preferred first-line antimicrobial for uncomplicated disease (Bass *et al.,* 1998) [4]. Despite this evidence, the overall benefit of antibiotic therapy in mild CSD remains modest, and many patients recover completely without specific antimicrobial treatment.

The therapeutic approach differs considerably in patients with disseminated or organ-specific disease. Ocular involvement, neurobartonellosis, infective endocarditis, osteomyelitis, hepatosplenic disease and other systemic manifestations generally require prompt antimicrobial therapy to prevent irreversible tissue damage. Several agents, including doxycycline, rifampin, azithromycin, erythromycin and gentamicin, have demonstrated activity against *Bartonella* species. Among these, the combination of doxycycline and rifampin is widely recommended for severe infections because both drugs achieve excellent intracellular penetration and provide complementary antimicrobial activity against this intracellular pathogen (Angelakis and Raoult, 2014) [2]. In cases of Bartonella-associated endocarditis treatment is often combined with prolonged antimicrobial administration and, when indicated, surgical intervention for management of valvular complications.

Patients with advanced immunosuppression require particular attention because they are at increased risk of disseminated disease, including bacillary angiomatosis and peliosis hepatis. These conditions generally respond to prolonged courses of doxycycline or macrolides; however, treatment often extends for several months to achieve complete clinical resolution. Premature discontinuation of therapy may result in relapse, especially in individuals with persistent immunodeficiency, emphasizing the importance of careful clinical follow-up.

Despite considerable advances in the clinical management of CSD, many therapeutic recommendations continue to rely on observational studies, case reports and expert opinion rather than robust randomized clinical trials. The rarity of severe disease, together with the diverse clinical presentations of *Bartonella* infection, has limited the availability of high-quality evidence to guide treatment. Future multicentre clinical studies are needed to establish standardized therapeutic protocols, define the optimal duration of antimicrobial therapy and evaluate newer treatment strategies for atypical and disseminated forms of cat scratch disease.

Prevention and Control

Preventing cat scratch disease (CSD) requires an integrated approach that targets the interconnected roles of reservoir hosts, arthropod vectors, human behavior and the shared environment. Since domestic cats serve as the principal reservoir of *Bartonella henselae*, effective prevention depends not only on reducing bacterial circulation within feline populations but also on minimizing opportunities for transmission to humans. These measures are most effective when implemented within a One Health framework that

combines veterinary care, public health education, and responsible pet ownership.

Among all preventive strategies, effective flea control remains the cornerstone of disease prevention. The cat flea (*Ctenocephalides felis*) plays a pivotal role in maintaining *Bartonella* transmission among cats, making vector control essential for interrupting the natural transmission cycle (Chomel *et al.,* 2006) [7]. Regular use of veterinarian-recommended ectoparasiticides substantially reduces flea infestations and lowers the prevalence of bacteremia in cats. Environmental management further complements these measures, with routine cleaning of pet bedding, carpets, upholstered furniture and other household areas helping to reduce flea populations and minimize the risk of reinfestation.

Equally important are simple behavioral measures that reduce human exposure. Individuals who own or frequently handle cats should be advised to wash scratches and bites promptly with soap and running water, maintain good hand hygiene after animal contact, and avoid rough play that may provoke scratching or biting, particularly with kittens. Because young cats are more likely to be bacteremic and heavily infested with fleas, careful handling of these animals is especially important. Immunocompromised individuals, including those with advanced HIV infection or receiving immunosuppressive therapy, should exercise additional caution by avoiding contact with flea-infested cats and seeking medical advice following potential exposure.

Veterinarians play a central role in the prevention of CSD through client education and routine preventive healthcare. Although healthy cats may remain persistently bacteremic without developing clinical illness, routine screening or antimicrobial treatment of asymptomatic animals is generally not recommended because it has limited value in eliminating infection and may contribute to unnecessary antimicrobial use. Instead, preventive veterinary practice should focus on year-round flea control, regular health assessments, promotion of responsible pet ownership and educating cat owners about practical measures that reduce zoonotic transmission.

Ultimately, sustained collaboration between veterinarians, physicians, public health authorities, and pet owners is essential for reducing the burden of cat scratch disease. Integrating vector control, public awareness, responsible animal management and timely clinical recognition offer the most effective strategy for limiting *Bartonella henselae* transmission while reinforcing the broader principles of the One Health approach.

One Health Perspective and Future Directions

Cat scratch disease (CSD) exemplifies the interconnected nature of human, animal, and environmental health and is increasingly recognized as a model One Health zoonosis. The epidemiology of *Bartonella henselae* is shaped by the dynamic interaction between reservoir hosts, arthropod vectors, environmental conditions, and human behavior. Rapid urbanization, expanding ownership of companion animals, increasing populations of free-roaming cats, and ecological changes that favor flea survival have collectively created conditions that facilitate the continued circulation of *Bartonella* within feline populations and increase opportunities for human exposure. Consequently, effective prevention and control cannot rely solely on medical intervention but require coordinated efforts across veterinary medicine, public health and environmental management.

Despite substantial progress in understanding *Bartonella* biology, several aspects of the disease remain poorly understood. The mechanisms responsible for persistent bacteremia in reservoir hosts, host susceptibility to severe disease and the pathogenesis of chronic and neurological manifestations require further investigation. Continued refinement of molecular diagnostic methods, whole-genome sequencing, and genomic epidemiology will improve strain characterization, enhance surveillance, and provide valuable insights into transmission dynamics across different geographical regions. Standardized diagnostic criteria and harmonized laboratory protocols are equally important for improving case detection and facilitating meaningful comparisons among epidemiological studies.

The development of effective preventive tools also represents a major research priority. Although experimental vaccine studies in cats have shown encouraging results, no licensed vaccine against *Bartonella henselae* is currently available. An effective feline vaccine could reduce reservoir infection, interrupt transmission within cat populations, and indirectly decrease the risk of human disease. Advances in vector biology, host immunity, and vaccine technology may therefore provide new opportunities for long-term disease prevention.

Future progress will depend on sustained collaboration among physicians, veterinarians, microbiologists, epidemiologists, entomologists, wildlife specialists, and public health professionals. Integrated One Health surveillance systems that combine clinical data, veterinary monitoring, vector surveillance, and molecular epidemiology will strengthen early detection, improve risk assessment, and support evidence-based control strategies. As human–animal interactions continue to evolve, adopting a comprehensive One Health approach will be essential for reducing the burden of cat scratch disease and improving the health of both people and companion animals.

Conclusion

Cat scratch disease (CSD) has emerged from being regarded as a relatively benign childhood illness to recognition as a globally important zoonotic infection with significant implications for human health, veterinary medicine, and public health. Increasing evidence accumulated over the past two decades has demonstrated that *Bartonella henselae* is capable of producing a remarkably diverse spectrum of clinical manifestations, ranging from localized lymphadenopathy to severe ocular, neurological, hepatosplenic, cardiovascular, musculoskeletal, and disseminated disease, particularly in immunocompromised individuals (Florin *et al.,* 2008; Angelakis and Raoult, 2014; Breitschwerdt *et al.,* 2024) [2, 6, 9]. This expanding clinical spectrum highlights the need for greater awareness among physicians and veterinarians, as delayed recognition may result in unnecessary investigations, inappropriate treatment, and preventable complications.

Advances in molecular biology have transformed current understanding of *Bartonella* epidemiology, host adaptation, and disease pathogenesis. The introduction of sensitive molecular diagnostic techniques, including polymerase chain reaction, multilocus sequence typing, and next-generation sequencing, has improved diagnostic accuracy, facilitated identification of atypical infections, and provided

new insights into the genetic diversity and transmission dynamics of *Bartonella* species (Harms and Dehio, 2012; McCormick *et al.,* 2023) [12, 14]. Nevertheless, important diagnostic challenges remain because of intermittent bacteremia, variable serological responses, and the limited availability of advanced molecular testing in many clinical settings. Continued efforts to standardize diagnostic protocols and expand access to molecular technologies will be essential for improving disease surveillance and patient management.

The epidemiology of CSD illustrates the close interdependence of human, animal, and environmental health. Domestic cats serve as the principal reservoir host, while the cat flea (*Ctenocephalides felis*) maintains bacterial transmission within feline populations. Human infection occurs largely through close interactions with infected animals, emphasizing that disease prevention depends not only on appropriate medical management but also on effective flea control, responsible pet ownership, public awareness, and routine veterinary preventive care (Chomel *et al.,* 2006; Guptill, 2010) [7, 11]. These interconnected factors firmly position CSD within the framework of the One Health concept, where coordinated collaboration between physicians, veterinarians, microbiologists, epidemiologists, entomologists and public health professionals is essential for effective disease prevention and control.

Despite considerable progress in understanding *B. henselae* biology, several important knowledge gaps remain. The mechanisms responsible for persistent bacteremia, host susceptibility to severe disease, chronic infection, and neurobartonellosis require further investigation. Future research should prioritize the development of standardized diagnostic algorithms, rapid point-of-care molecular assays, genomic surveillance, improved understanding of host–pathogen interactions, and the identification of novel therapeutic targets. In addition, continued research into feline vaccines and innovative vector-control strategies may provide sustainable approaches for interrupting transmission and reducing the overall burden of infection (Barbour *et al.,* 2023; Breitschwerdt *et al.,* 2024) [6].

In conclusion, cat scratch disease should no longer be viewed as a simple cause of regional lymphadenitis but rather as a complex and evolving zoonosis with important clinical and public health consequences. As human–animal interactions continue to intensify and environmental factors increasingly influence vector ecology, the importance of integrated surveillance and multidisciplinary collaboration will continue to grow. Strengthening One Health partnerships, improving diagnostic capacity, promoting responsible companion animal management, and expanding research on *Bartonella* pathobiology will be fundamental to reducing the global impact of this neglected yet increasingly recognized zoonotic infection and safeguarding the health of both humans and animals (Chomel *et al.,* 2006; Florin *et al.,* 2008[7, 9]; McCormick *et al.,* 2023; Breitschwerdt *et al.,* 2024) [6].

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