Cat Scratch Disease and Other *Bartonella* Infections

13

Kenneth M. Zangwill

Abstract

First described in 1931, cat scratch disease remains the most commonly identified clinical syndrome associated with *Bartonella* infection. Over the last 20 years, however, the discovery and use of modern diagnostic tests has greatly expanded our understanding of the pathogenesis, clinical spectrum, and treatment options for *Bartonella* infections of all types. Indeed, each varies substantially depending on the infecting species and the immune status of the host.

13.1 Introduction

Bartonella species cause a wide range of clinical syndromes which vary substantially depending on the infecting species and immune status of the infected. Well known as a cause of trench fever and bartonellosis (a febrile illness endemic in the high valleys of the Andes mountains [1]), their recognition as human pathogens in the United States was virtually forgotten until the early 1990s when new diagnostic tests linked this genus to cat scratch disease. Today, the use of such tests has significantly broadened the clinical spectrum of cat scratch disease and also confirmed the role of *Bartonella* as the cause of bacillary angiomatosis (BA), an entity seen mainly among the immunocompromised.

K. M. Zangwill (✉)
Pediatric Infectious Diseases, David Geffen School of Medicine at UCLA, Harbor-UCLA Medical Center, Los Angeles, USA
e-mail: kzangwill@uclacvr.labiomed.org

13.2 Making the Link Between *Bartonella* and Cat Scratch Disease

Cat scratch disease (CSD) was first described in a French boy seen in 1931 [2], but > 50 years elapsed before evidence of its bacterial cause emerged. In 1983, Warthin-Starry staining revealed small bacilli among 34 of 39 lymph node samples from patients with CSD and in subcutaneous nodules from a patient with AIDS with unusual neovascular lesions subsequently recognized as BA [3, 4]. In 1988, it was proposed that CSD and BA may result from infection by the same organism based on the similarity of the morphologic and staining characteristics of these bacilli and that a history of cat scratches was often present in these patients. Importantly, antiserum raised against the "CSD bacillus" reacted with organisms in tissue samples from BA patients [5].

In 1990, molecular probe techniques (polymerase chain reaction (PCR)) suggested that BA

N. Curtis et al. (eds.), *Hot Topics in Infection and Immunity in Children IX,*
Advances in Experimental Medicine and Biology 764, DOI 10.1007/978-1-4614-4726-9_13,

was caused by a bacterium similar to *Bartonella quintana* [6]. Other reports described morphologically similar-appearing organisms from patients with a vascular abnormality of the liver known as peliosis hepatitis [7] and febrile bacteremia [8], subsequently noted to be caused by both *B. quintana* and *B. henselae* [9–12]. Soon thereafter, a newly developed immunofluorescent antibody serologic test developed for BA was positive in 36 of 41 (88 %) serum samples from persons with suspected CSD, compared with only 6 % among healthy controls [13]; findings soon corroborated in a field trial among CSD patients in Connecticut, USA [14]. During this time, it was reported that CSD skin test antigen contained *Bartonella* nucleic acid sequences [15]. These observations confirmed the etiologic link between *Bartonella* and CSD and BA. Subsequently, organisms have been visualized microscopically or detected using PCR at the site of skin inoculation, lymph nodes, bone, eye, liver, and spleen in patients with CSD [16–21] and in nearly every organ, including the brain, among those with BA [22]. Regardless, the organism is only infrequently successfully cultured from clinical specimens among patients with either of these conditions.

13.3 Pathogenesis

Bartonella are facultative, intracellular Gram-negative bacilli with relatively fastidious growth characteristics. To maximize growth, tissue samples ideally should be directly plated onto solid media supplemented with hemin and incubated in a hypercapneic atmosphere. Most standard protocols for detection of such fastidious bacteria will allow for growth of *Bartonella*, but only after at least 7–10 days of incubation [23]. Currently at least 22 species have been described, 12 are known to cause disease in humans and the complete genome is available for 10 separate species.

In general, *Bartonella* establish infection within the reservoir host and eventually establish persistence within the erythrocyte. Several observations suggest that *Bartonella* may persist intracellularly: (1) persistent bacteremia has been noted in humans and a variety of mammals, (2) isolation is enhanced by lysis centrifugation (which disrupts cellular membranes), (3) BA and trench fever patients may experience clinical relapse, and (4) better clinical response has been noted with antimicrobial agents that penetrate intracellularly. The defining pathogenic characteristics of human infection vary substantially with the infecting *Bartonella* species and also with immune status of the host. Transmission to humans can occur directly via an arthropod vector (e.g. sandflies and bartonellosis) or indirectly via inoculation (perhaps from infected flea feces) through intact skin via a cat scratch or other mucous membrane contact (CSD and BA). Many virulence factors involved in human infection have been identified that contribute to cellular invasion, erythrocyte persistence, pathologic angiogenesis, and evasion from host immune responses. A comprehensive review of *Bartonella* pathogenetic mechanisms has been recently published [24].

These primary clinical histopathologic manifestations range from focal granulomatous changes (CSD), multifocal angioproliferative changes (BA), endovascular multiplication (endocarditis), and an (proposed) exaggerated inflammatory response without evidence of bacterial invasion (meningoencephalitis). In CSD specifically, the lymph node histology reveals patchy, necrotic, granulomatous change with stellate abscesses and variable infiltration of leukocytes. This is in contrast to BA which typically reveals proliferation of small blood vessels with large, "plump" cuboidal endothelial cells with intermixed leukocyte infiltration and focal necrosis without granulomas, similar to that seen with bartonellosis.

13.4 Ecology

Various reservoirs for *Bartonella* species have been identified including feline, bovine, canine, cetacean, and rodent species. Most individual species, however, are relatively restricted in their distribution. Epidemiologic studies of patients with CSD and BA have shown that contact with cats, particularly kittens in the case of CSD, is associ-

ated with disease [14, 25]. Cats from households of such patients are more likely to have antibody against *B. henselae* than are control cats, seroprevalence of anti-*Bartonella* antibody among community cats can be very high (depending on the region) and overt feline bacteremia among community cats may exceed 50 % persisting for up to a year [14, 26–29]. Younger cats and stray cats are more likely to be infected with *Bartonella* than are older or domesticated cats [30].

It appears that each pathogenic *Bartonella* species may be transmitted by an arthropod vector, with variation by species. These vectors include flies, fleas, keds, lice, sandflies, and ticks, but most infections appear to be accidental in animal and human hosts. *B. quintana* and *B. bacilliformis* are transmitted by the human body louse and the sandfly, respectively. For *B. henselae,* the cat flea (*Ctenocephalides felis*) has been confirmed as a vector for CSD and/or BA through epidemiologic [14, 25] and experimental [14, 27, 31, 32] evidence. These data show that cat fleas can harbor *Bartonella* as detected by culture and PCR, cats bacteremic with *B. henselae* are more likely than nonbacteremic cats to be infested with fleas, and fleas can successfully transmit to *Bartonella* cats in a laboratory setting.

13.5 Cat Scratch Disease

Although definitive evidence is not available, it appears that the majority of infections caused by *Bartonella* species result in CSD, usually due to *B. henselae*. Large case series and systematic evaluations have defined the epidemiology of CSD. United States population-based surveillance data indicate that the incidence over all age groups is 3–4 per 100,000 population. Approximately 60 % of cases occur in persons < 18 years of age with children 5–10 years of age at greatest risk (~ 10 per 100,000 population) [14, 33]. Familial and geographic clusters have been reported and incidence peaks in the winter months, with some geographic variability. Hospitalization for this illness occurs most commonly for surgical drainage or excision of affected lymph nodes with an annual incidence of ~ 0.6/100,000 children < 18 years of age in the United States [34]. A case-control evaluation noted that owning a kitten and being scratched, bitten, or licked by a kitten with fleas are the most important risk factors for disease [14]. Nearly 25 % of persons with CSD, however, do not report intimate contact with cats, though person-to-person transmission has not been documented.

Table 13.1 Cat scratch disease: classic manifestations. (Data from [14, 38, 46, 66]

Clinical finding	Percent of patients
Lymphadenopathy	> 90
Upper extremity	46–52
Neck/jaw	26–43
Groin	6–18
Suppuration	15–30
Fever	26–60
Inoculation site detectable	25–90
Malaise/fatigue/anorexia/ headache	10–45
Myalgia/arthropathy/tendinitis	3–11
Parinaud oculoglandular syndrome	5
Skin rash/erythema nodosum	3–5
Encephalopathy	< 1

Uncomplicated CSD is usually a self-limited illness characterized by lymphadenopathy that occurs after contact with a cat. A few days after a cat-scratch or bite, a papule or wheal frequently develops at the site which is followed by development of regional lymphadenopathy 1–2 weeks later. Concomitant constitutional symptoms occur in up to 60 % of cases including malaise, fever, sore throat, and/or headache (Table 13.1). Children < 15 years of age are more likely to develop lymphadenopathy in the neck, whereas older persons are more likely to have enlarged nodes in the groin or axilla [33]. Up to one-third of patients will report lymphadenopathy at more than one site. Nodes generally are not tender, yet suppuration occurs in 15–30 % of cases with even deep neck space disease reported [35]. Prolonged bacteremia and even widespread dissemination involving multiple organ systems has been reported as well [36, 37]. In most cases of CSD, the clinical illness resolves spontaneously but lymphadenopathy may persist for weeks to months [38].

The widespread use of a serologic test against *Bartonella* species has rapidly and significantly expanded the clinical spectrum of this illness to include nearly every organ system. Delays in diagnosis are commonplace and occur most likely due to general lack of awareness with the potential for infection among patients who have a non-classic presentation. Central nervous system disease most commonly presents as encephalopathy with associated seizures in 40–50 % of patients [21]. Status epilepticus, cranial and peripheral nerve paresis, and intracranial masses also have been reported. Onset is usually 1–2 months after the development of lymphadenopathy, and complete and rapid recovery is the rule, but severe disease with sequelae may occur [21, 39, 40]. Cerebrospinal fluid analysis is usually normal, but lymphocytic pleocytosis is noted in approximately one-third of patients. Ophthalmic disease usually presents as Parinaud oculoglandular syndrome (bulbar conjunctivitis, preauricular lymphadenopathy, and conjunctival granuloma), but other manifestations are well-described and neuroretinitis in the form of a "macular star" is particularly distinctive [41, 42]. Hepatitis and/or splenitis is well-described as well, usually accompanied by prolonged fever, abdominal pain, arthralgias, and/or pleomorphic rashes. Back pain is a common presenting symptom in such children [43–45]. In addition, many patients have been reported with musculoskeletal disease (particularly in women >20 years of age) or osteomyelitis with vertebral disease and contiguous abscess formation being prominent [46, 47]. Pulmonary disease has also been described in which nearly all patients developed pleural effusion [48]. The majority of patients with non-classic disease recover completely, and no deaths have been directly attributable to CSD. Clinical disease appears to provide lifelong protection insofar as recurrent disease has been described very rarely [43].

13.6 Bacillary Angiomatosis

BA is an uncommon manifestation of *B. henselae* or *B. quintana* infection seen primarily in adults with acquired immunodeficiency, usually during the late stages of AIDS [22]. The incidence and seasonal distribution of BA is unknown. Being scratched or bitten by a cat has been established as a risk factor for BA, but overall, one-third of patients did not report such contact in one study [25]. The clinical manifestations of BA are quite varied and may involve nearly every organ system but cutaneous, osseous, hepatic (peliosis hepatis), and splenic disease are the most commonly reported [22]. The range of cutaneous disease is broad, usually including superficial, erythematous, highly vascular, exophytic lesions or subcutaneous nodules. Lesions occur singly, or hundreds of lesions may occur in the same patient. Bone disease usually is painful and localized to tubular bones, with osteolysis noted on roentgenogram. Hepatosplenic disease often presents with prolonged fever, abdominal pain, and substantial weight loss. Only a few instances of BA have been reported among children some of whom were immunocompetent [49–51].

13.7 Other Syndromes

In addition to "classic" CSD and BA, *Bartonella* species have been linked to several other syndromes. *B. quintana* and *B. henselae* bacteremia, most commonly seen among the homeless or those infested with scabies or lice, may persist for prolonged periods despite antimicrobial therapy [8, 11, 12, 52]. Endocarditis caused by several *Bartonella* species has been described and now should be included as a potential cause of "culture-negative" HACEK-type endocarditis, i.e., endocarditis caused by fastidious Gram-negative organisms. Such patients usually have one or more underlying conditions, including infection with HIV, chronic alcoholism, or homelessness [53–56]. The homelessness and infestations associated with *Bartonella* infection noted above parallel conditions experienced by soldiers with trench fever in which prolonged bacteremia with *B. quintana* was also reported.

Lastly, *Bartonella* have been implicated in several different central nervous system syndromes which may represent rare forms of CSD or BA, or unique manifestations of *Bartonella* infection altogether. These syndromes, most frequently noted in patients with HIV infection,

include aseptic meningitis, transient cranial and/or peripheral nerve dysfunction, aphasia, alteration in mood or affect, psychoses, space-occupying lesions, and an acute psychiatric complex [41, 57, 58].

13.8 Diagnosis

The approach to diagnosis of infection with *Bartonella* varies with the clinical presentation. For classic CSD, particularly in immunocompetent hosts, the diagnosis can usually be confidently made with the subacute emergence of regional lymphadenopathy with or without constitutional symptoms in persons with prior traumatic contact with a cat or kitten distal to the affected node. In such instances, serologic testing, molecular diagnostics, or imaging is usually unnecessary.

Other *Bartonella* syndromes, however, require the use of serologic testing or clinical specimens for microbiologic and/or molecular evaluations. Currently, serologic testing is the mainstay of diagnosis and is most commonly done using a commercially available enzyme immunoassay or an indirect immunofluorescence assay for *Bartonella* IgM and IgG antibody levels. The sensitivity of these tests is variable and may be low, but specificity is generally quite high [59, 60]. Among patients with CSD, antibody titers peak at 4–5 months after onset of symptoms and have been shown to persist for up to 3 years [14, 61]. Serologic tests have completely supplanted the use of the CSD skin test, a non-standardized preparation previously available in limited quantities, originally developed in 1946 [2]. Currently available serologic tests are not able, however, to differentiate reliably between species of *Bartonella*. Molecular techniques are also available in many commercial laboratories, but the methods are not standardized.

Bartonella species are relatively fastidious and recovery is maximized with the use of lysis centrifugation technique and selective media that contain hemin, followed by growth in a hypercapnic atmosphere for at least 10 days. Tissue samples may reveal *Bartonella* with the use of a range of silver stains and Gram's stain is generally insensitive for this pathogen.

13.9 Therapy

The majority of mild-to-moderate cases of CSD resolve in 1–2 months without any antimicrobial therapy. Although *Bartonella* species appear to be susceptible to several antimicrobials when tested *in vitro*, such results do not predict reliably the clinical response to therapy; use of such tests as a clinical tool should therefore be discouraged.

Only one prospective controlled study of therapy for cat scratch disease has been published [62]. This study reported on 29 patients who were randomized to azithromycin (for 5 days) or placebo after diagnosis was confirmed by serologic testing. The outcome measure was change in the (largest) lymph node size, as determined by ultrasound 30 days after initiation of treatment. No other clinical signs or symptoms were reported and drug compliance was not monitored. The authors note that those in the treatment group had significant improvement in nodal size and suggested that azithromycin be considered for therapy of this condition.

This study, however, was flawed in several important areas rendering its conclusions highly suspect [63]. There were only 14–15 patients per group, >50 % of whom in each group received at least one antimicrobial before randomization and the details of type and duration of antimicrobial use are not presented. Very little information was presented with regard to clinical resolution of signs and symptoms (aside from the ultrasound data) and interestingly there was little correlation between physical examination and findings on ultrasonography of lymph nodes. As well, the authors report a statistically significant difference in nodal size at 30 d, but this difference was not present by 60 d. The clinical relevance of the ultrasonographic findings, specifically for deciding about the need for antimicrobial therapy in the absence of demonstrable clinical benefit, is unclear. Anecdotal evidence and retrospective series suggest that some clinical response may be achieved for patients with CSD with trimethoprim-sulfamethoxazole, rifampin, gentamicin, and in adults, ciprofloxacin.

A combination of therapeutic restraint, pain control, and reassurance remains the most

prudent approach to the great majority of patients with uncomplicated CSD in whom clinical symptoms and signs, as well as lymphadenopathy, will likely spontaneously resolve over several weeks to months. Antimicrobial therapy may be considered for those patients (1) in whom lymphadenopathy does not resolve over a reasonable period, (2) in whom lymphadenopathy is associated with significant morbidity, such as pain or persistence of debilitating constitutional symptoms, (3) with severe systemic disease; i.e., encephalopathy, osteomyelitis, or neuroretinitis, and/or (4) with an underlying medical disorder complicated by severe CSD. Specific recommendations for these circumstances cannot be definitive as controlled data are unable, but an expert panel has published guidelines [64].

Aspiration of inflamed lymph nodes only should be performed to rule out more serious diagnoses or if a treatable superinfection is suspected. In such cases, either a fine-needle aspiration or excisional biopsy should be done; incision and drainage procedures may promote the development of fistulae. No specific measures regarding antimicrobial prophylaxis of close contacts of the implicated cat itself can be recommended. Also, declawing of the cat or its removal from the household is not necessary.

Patients with BA usually respond to macrolides or tetracyclines. Uncomplicated cutaneous disease in HIV-infected patients requires at least 6–8 weeks of therapy, whereas more severe or invasive disease may require months of therapy or perhaps lifetime suppressive therapy. Others have proposed specific treatment regimens for BA, bacteremia, and endocarditis caused by *Bartonella* that include various combinations of gentamicin, erythromycin, or ceftriaxone [64].

13.10 Opportunities

With the wide availability of serologic and molecular diagnostic tools, new information about *Bartonella* infections will likely continue to emerge. Important knowledge gaps remain in nearly all domains of this organism as a human pathogen including the dynamics of its ecology and transmission in nature, human pathogenesis, relationship of the host to the pathogen, and differing responses to antimicrobial therapy. Cats remain the most important reservoir for CSD and BA—and over one-third of all U.S. households include at least one cat [65]—perhaps new information will lead to a preventive approach such as vaccination of cats.

References

1. Garcia-Caceres U, Barcia FU (1991) Bartonellosis: an immunodepressive disease and the life of Daniel Alcides Carrion. Am J Clin Pathol 95(Supp 1):558–566
2. Carithers H (1970) Cat-scratch disease. Notes on its history. Am J Dis Child 119:200–203
3. Wear DJ, Margileth AM, Hadfield TL et al (1983) Cat-scratch disease: a bacterial infection. Science 225:1403–1405
4. Stoler MH, Bonfiglio TA, Steigbigel RT et al (1983) An atypical subcutaneous infection associated with acquired immune deficiency syndrome. Am J Clin Pathol 80:714–718
5. LeBoit PE, Berger TG, Egbert BM et al (1988) Epithelioid haemangioma-like vascular proliferation in AIDS: manifestation of cat-scratch disease bacillus infection? Lancet 1:960–963
6. Relman DA, Loutit JS, Schmidt TM et al (1990) The agent of bacillary angiomatosis: an approach to the identification of uncultured pathogens. N Engl J Med 323:1573–1580
7. Perkocha, LA, Geaghan SM, Yen TSB et al (1990) Clinical and pathological features of bacillary peliosis hepatis in association with human immunodeficiency virus infection. N Engl J Med 323:1581–1586
8. Slater, LN, Welch DF, Hensel DH et al (1990) A newly recognized fastidious gram-negative pathogen as a cause of fever and bacteremia. N Engl J Med 32:1587–1593
9. Relman DA, Falkow S, Le Boit PE et al (1991) The organism causing bacillary angiomatosis, peliosis hepatis, and fever and bacteremia in immunocompromised patients. N Engl J Med 324:1514
10. Welch DF, Pickett DA, Slater LN et al (1992) *Rochalimaea henselae* sp. nov., a cause of septicemia, bacillary angiomatosis, and parenchymal bacillary peliosis. J Clin Microbiol 30:275–280
11. Lucey D, Dolan M, Moss CW et al (1992) Relapsing illness due to *Rochalimaea henselae* in immunocompetent hosts: implication for therapy and new epidemiological associations. Clin Infect Dis 14:683–688
12. Regnery RL, Anderson BE, Clarridge JE et al (1992) Characterization of a novel *Rochalimaea* species, *R. henselae* sp. nov., isolated from blood of a febrile,

human immunodeficiency virus-positive patient. J Clin Microbiol 30:265–274
13. Regnery RL, Olson JG, Perkins BA et al (1992) Serological response to *"Rochalimaea henselae"* antigen in suspected cat-scratch disease. Lancet 339:1443–1445
14. Zangwill KM, Hamilton DH, Perkins BA et al (1993) Cat-scratch disease in Connecticut: epidemiology, risk factors and evaluation of a new diagnostic test. N Engl J Med 329:8–13
15. Anderson B, Kelly C, Threlkel R et al (1993) Detection of *Rochalimaea henselae* in cat scratch disease skin test antigens. J Infect Dis 168:1034–1036
16. Margileth AM, Wear DJ, Hadfield TL et al (1984) Cat-scratch disease: bacteria at the primary inoculation site. JAMA 252:928–931
17. Anderson B, Sims K, Regnery R et al (1994) Detection of *Rochalimaea henselae* DNA in specimens from cat-scratch disease patients by PCR. J Clin Microbiol 32:942–948
18. Demers DM, Bass JW, Vincent JM et al (1995) Cat-scratch disease in Hawaii: etiology and seroepidemiology. J Pediatr 127:23–36
19. Waldvogel K, Regnery R, Anderson B et al (1994) Disseminated cat-scratch disease: detection of *Rochalimaea henselae* in affected tissue. Eur J Pediatr 153:23–27
20. Le HH, Palay DA, Anderson B, Steinberg JP (1994) Conjunctival swab to diagnose ocular cat-scratch disease. Am J Ophthalmol 118:249–250
21. Carithers HA, Margileth AM (1991) Cat-scratch disease: acute encephalopathy and other neurologic manifestations. Am J Dis Child 145:98–101
22. Koehler JE, Tappero JW (1993) Bacillary angiomatosis and bacillary peliosis in patients infected with human immunodeficiency virus. Clin Infect Dis 17:612–624
23. Welch DF, Hensel RM, Pickett DA et al (1993) Bacteremia due to *Rochilimaea henselae* in a child: practical identification of isolates in the clinical laboratory. J Clin Microbiol 31:2381–2386
24. Harms A, Dehio C (2012) Intruders below the Radar: molecular pathogenesis of *Bartonella* spp. Clin Microbiol Rev 25:42–78
25. Tappero JW, Mohle-Boetani J, Koehler JE et al (1993) The epidemiology of bacillary angiomatosis and bacillary peliosis. JAMA 269:770–775
26. Jameson P, Greene C, Regnery R et al (1995) Prevalence of *Bartonella henselae* antibodies in pet cats through the regions of North America. J Infect Dis 172:1145–1149
27. Koehler JE, Glaser CA, Tappero JW (1994) *Rochalimaea henselae* infection: a new zoonosis with the domestic cat as reservoir. JAMA 271:531–535
28. Breitschwerdt E, Kordick DL (2000) *Bartonella* infection in animals; carriership, reservoir potential, pathogenicity, and zoonotic potential for human infection. Clin Microbiol Rev 13:428–438
29. Kordick DL, Wilson KH, Sexton DJ et al (1995) Prolonged *Bartonella* bacteremia in cats associated with cat-scratch disease. J Clin Microbiol 33:3245–3251
30. Chomel BB, Abbott RC, Chasten RW et al (1995) *Bartonella henselae* prevalence in domestic cats in California: risk factors and association between bacteremia and antibody titers. J Clin Microbiol 33:2445–2450
31. Chomel BB, Kasten RW, Floyd-Hawkins KF et al (1996) Experimental transmission of *Bartonella henselae* by the cat flea. J Clin Microbiol 34:1952–1956
32. Rolain JM, Franc M, Davoust B, Raoult D (2003) Molecular detection of *Bartonella quintana, B. koehlerae, B. henselae, B. clarridgeiae, Rickettsia felis,* and *Wolbachia pipientis* in cat fleas, France. Emerg Infect Dis 9:338–342
33. Hamilton DH, Zangwill KM, Hadler JL et al (1995) Cat-scratch disease—Connecticut,1992–1993. J Infect Dis 172:570–573
34. Reynolds MG, Homan RC, Curns AT et al (2005) Epidemiology of cat-scratch disease hospitalizations among children in the United States. Pediatr Infect Dis J 24:700–704
35. Yeh SH, Zangwill KM, Hall B, McPhaul L, Keller M (2000) Parapharyngeal abscess due to cat- scratch disease. Clin Infect Dis 30:599–601
36. Arvand M, Schad SG (2006) Isolation of *Bartonella henselae* DNA from the peripheral blood of a patient with cat scratch disease up to 4 months after the cat scratch injury. J Clin Microbiol 44:2288–2290
37. Waldvogel K, Regnery R, Anderson BE et al (1994) Disseminated cat-scratch disease: detection *Rochalimaea henselae* in affected tissue. Eur J Pediatr 153:23–27
38. Carithers HA (1985) Cat-scratch disease: an overview based on a study of 1200 patients. Am J Dis Child 193:1124–1133
39. Selby G, Walker GL (1979) Cerebral arteritis in cat-scratch disease. Neurology 29:1413–1418
40. Wong M, Isaacs D, Dorney S (1995) Fever, abdominal pain and an intracranial mass. Pediatr Infect Dis J 14:725–728
41. Wong MT, Doan MJ, Lattuada CP et al (1995) Neuroretinitis, aseptic meningitis, and lymphadenitis associated with *Bartonella (Rochalimaea) henselae* infection in immunocompetent patients and patients infected with human immunodeficiency virus type 1. Clin Infect Dis 21:352–360
42. Roe RH, Michael Jumper J, Fu AD et al (2008) Ocular *Bartonella* infections. Intl Ophthal Clin 48:93–105
43. Margileth AM, Wear DJ, English CK (1987) Systemic cat-scratch disease: report of 23 patients with prolonged or recurrent severe bacterial infection. J Infect Dis 155:390–402
44. Rappaport DC, Cumming WA, Ros PR (1991) Disseminated hepatic and splenic lesions in cat-

scratch disease: imaging features. Am J Roentgenol 156:1227–1228
45. Malatack JJ, Jaffe R (1993) Granulomatous hepatitis in three children due to cat-scratch disease without peripheral adenopathy. Am J Dis Child 147:949–953
46. Maman E, Bickels J, Ephros M et al (2007) Musculoskeletal manifestations of cat scratch disease. Clin Infect Dis 45:1535–1540
47. Hajjaji N, Hocqueloux L, Kerdraon R, Bret L (2007) Bone infection in cat-scratch disease: a r eview of the literature. J Infect 54:417–421
48. Margileth AM, Baehren DF (1998) Chest-wall abscess due to cat-scratch disease (CSD) in an adult with antibodies to *Bartonella* clarridgeiae: case report and review of the thoracopulmonary manifestations of CSD. Clin Infect Dis 27:353–357
49. Myers SA, Prose NS, Garcia JA et al (1992) Bacillary angiomatosis in a child undergoing chemotherapy. J Pediatr 121:574–578
50. Malane MS, Laude TA, Chen CK et al (1995) An HIV-1-positive child with fever and a scalp nodule. Lancet 346:1466
51. Zarraga M, Rosen L, Herschthal D (2011) Bacillary angiomatosis in an immunocompetent child: a case report and review of the literature. Am J Dermatopath 33:513–515
52. Ohl ME, Spach DH (2000) *Bartonella* quintana and urban trench fever. Clin Infect Dis 31:131–135
53. Drancourt M, Birtles R, Chaumentin G et al (1996) New serotype of *Bartonella henselae* in endocarditis and cat-scratch disease. Lancet 347:552–554
54. Spach DH, Kanter AS, Daniels NA et al (1995) *Bartonella (Rochalimaea)* species as a cause of apparent "culture-negative" endocarditis. Clin Infect Dis 20:1044–1047
55. Drancourt M, Mainardi JL, Brouqui P et al (1995) *Bartonella (Rochalimaea) quintana* endocarditis in three homeless men. N Engl J Med 332:419–423
56. Daly JS, Worthington MG, Brenner DJ et al (1993) *Rochalimaea elizabethae* sp. nov. isolated from a patient with endocarditis. J Clin Microbiol 31:872–881
57. Schwartzman WA, Patnaik M, Barka NE et al (1994) *Rochalimaea* antibodies in HIV- associated neurologic disease. Neurology 44:1312–1316
58. Baker J, Ruiz-Rodriquez R, Whitfield M et al (1995) Bacillary angiomatosis: a treatable cause of acute psychiatric symptoms in human immunodeficiency virus infection. J Clin Psychiatry 56:161–166
59. Hoey JG, Valois-Cruz F, Goldenberg H et al (2009) Development of an immunoglobulin M capture-based enzyme-linked immunosorbent assay for diagnosis of acute infections with *Bartonella henselae*. Clin Vaccine Immunol 16:282–284
60. Vermeulen MJ, Verbakel H, Notermans DW, Reimerink JH, Peeters MF (2010) Evaluation of sensitivity, specificity and cross-reactivity in *Bartonella henselae* serology. J Med Microbiol 59:743–745
61. Metzkor-Colter E, Kletter Y, Avidor B et al (2003) Long-term serological analysis and clinical follow-up of patients with cat scratch disease. Clin Infect Dis 37:1149–1154
62. Bass JW, Freitas BC, Freitas AD et al (1998) Prospective randomized double blind placebo—controlled evaluation of azithromycin for treatment of cat-scratch disease. Pediatr Infect Dis J 17:447–452
63. Zangwill KM (1998) Therapeutic options for cat-scratch disease. Pediatr Infect Dis J 17:1059–1061
64. Rolain JM, Brouqui P, Koehler JE et al (2004) Recommendations for treatment of human infections caused by *Bartonella* species. Antimicrob Agents Chemother 48:1921–1933
65. http://www.humanesociety.org/issues/pet_overpopulation/facts/pet_ownership_statistics.html. Accessed 5 Feb 2012
66. Margileth AM (1968) Cat scratch disease: nonbacterial regional lymphadenitis. The study of 145 patients and a review of the literature. Pediatrics 42(5):803–818 (http://www.ncbi.nlm.nih.gov/pubmed/4972192)