Cat-scratch Disease: Epidemiology, Etiology, and Treatment

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Cat-scratch disease (CSD) is a clinical syndrome that usually presents as a self-limiting lymphadenopathy associated with a cat scratch or bite. Commonly affecting children and young adults, it has a worldwide distribution. In temperate climates, higher rates are reported in the autumn and winter, which can be attributed to the seasonal breeding of the domestic cat. The organism responsible was identified in 1983, having eluded detection for 50 years. Initially, *Afipia felis* was thought to be the cause, however, subsequent study failed to confirm a link. During the 1990s, it was demonstrated conclusively that *Rochalimaea henselae*, later reclassified as *Bartonella henselae*, was the cause of CSD. *B. henselae* has been isolated from bacteremic cats, with transmission among cats thought to be via the cat flea. Although other *Bartonella* species are transmitted by arthropod vectors, it is unlikely that the cat flea is involved directly in human infection, but plays a role in amplifying the reservoir. *B. henselae* is difficult to culture, and either serology or the polymerase chain reaction are considered to be the best methods of detection. Genetic variation occurs among *B. henselae* strains, perhaps explaining the inconsistency of some diagnostic techniques. A separate serogroup (Marseilles) has been reported in a seronegative patient with CSD, and *B. clarridgeiae* has the potential to cause the disease. Atypical presentation is seen in up to 25% of cases, and manifests itself as ocular involvement, encephalopathy, granulomatous hepatitis, hepatosplenic infection, endocarditis, and osteomyelitis. The majority of CSD cases resolve spontaneously and do not require antibiotic treatment. In complicated CSD, treatment with trimethoprim-sulphamethoxazole, ciprofloxacin, or azithromycin is recommended, with gentamicin being reserved for the severely ill patient.

Introduction

Cat-scratch disease (CSD) is characterized usually as a self-limiting regional lymphadenopathy, associated with a cat scratch or bite. Although CSD is normally benign, the causative organism(s) may cause severe systemic or recurrent disease. Originally considered rare, it is now recognized to affect children and young adults commonly, and occurs worldwide. Indeed, in some areas it is the most common cause of chronic lymphadenopathy in this age group. CSD occurs more frequently in certain geographical areas and shows a marked seasonality. In the USA, it is estimated that over 24,000 cases occur annually, with 2,000 patients requiring hospitalization, and a resulting health-care expenditure of $12 million.

Despite many clinical descriptions (750 by the early 1980s), the etiological agent remained elusive. Various organisms have been implicated since the early 1900s, including viruses, chlamydia, acid-fast bacilli, and gram-positive bacteria and it was not proven to be a bacterial infection until 1983. However, the isolation and characterization of the causative organism(s) would prove to be more difficult. Indeed, it is only in the past decade, using powerful molecular techniques, that the true etiological picture has emerged.

Historical overview

CSD was described initially by Debré and coworkers in 1950, although Parinaud is credited with the first report of symptoms consistent with CSD some 60 years earlier, when he described Parinaud's oculoglandular syndrome in 1889. Debré examined his first patient, a 10-year-old boy who presented with suppurative adenitis and severe cat scratches, in 1931.

Although physicians in the USA were aware of patients with CSD as early as 1932, the first published American case was not reported until 1951. Foshay, a professor of microbiology at the University of Cincinnati, produced a crude intradermal skin test in 1947. The antigen used was derived from pus obtained from the lymph nodes of individuals suspected of having the disease.

Professor Mollaret, at the Pasteur Institute, studied CSD independently, and also prepared a skin antigen test. Many extensive clinical reviews followed, including Warwick's description of 160 cases in 1960, and Carithers' review of 1,200 cases, published in 1985. Surprisingly, the clinical description of CSD changed little over the decades. To date, over 900 publications have appeared in the scientific literature, reflecting the high level of interest shown in this intriguing syndrome.

**Etiology**

The etiological agent of CSD eluded detection for 50 years. Although many infectious agents were suspected, it was not until 1983 that Wear and coworkers demonstrated that it was a bacterial infection. Using the Warthin-Starkey silver stain, they detected small, delicate pleomorphic bacilli in 34 out of 39 lymph nodes taken from patients with suspected CSD. Using an immunoperoxidase staining technique, the organisms in sections of lymph node stained intensely when exposed to convalescent sera from CSD patients, whereas they did not react with control sera.

These results were supported by the work of Margileth and coworkers, who used the same staining methods and detected bacilli in both biopsies of inoculation papules and the lymph nodes draining the site of inoculation in CSD patients.

In 1988, English and coworkers isolated a bacterial organism from the lymph nodes of ten patients with CSD, after extended incubation on specialized media. After inoculation into a nine-banded armadillo, it caused dermal lesions identical to those seen in humans. The group was able to reisolate the organism from these lesions, thereby fulfilling Koch's postulates, and considered it to be the causative agent of CSD.

Initially, it was known simply as the "cat-scratch disease bacillus." However, in 1991, when Brenner and coworkers described the genus *Afipia*, it was given the specific name *Afipia felis*. *Afipia* was taken from the Armed Forces Institute of Pathology, where the original organism was isolated; and *felis* referred to the cat as the probable vector. Subsequent reports failed to confirm a strong link between *A. felis* and CSD, however. Indeed, further doubt was cast when patients with CSD failed to mount either a humoral or cellular response to *A. felis* antigen. In addition, other investigators were unable to isolate *A. felis* from CSD patients; and, despite most patients reporting exposure to cats, no clear link could be demonstrated between cats and *A. felis*.

In 1990, Relman and coworkers using a novel method for identifying uncultured pathogens, identified the causative agent of bacillary angiomatosis (BA). This is an infectious disease that causes cutaneous lesions, and primarily affects human immunodeficiency virus (HIV)-positive patients. The organism was visualized previously in infected tissue stained using the Warthin-Starkey method, and looked similar to that associated with CSD.

Using the polymerase chain reaction (PCR), this group amplified prokaryotic 16S ribosomal RNA (rRNA) gene products directly from tissue samples. The primers used were common to all bacteria, and the amplified DNA was sequenced and found to be related to *Rochalimaea quintana*.

At the same time, in Oklahoma, Slater and coworkers isolated Rochalimaea-like organisms from the blood of two HIV-positive patients presenting with persistent fever. Similar organisms were isolated subsequently from blood and lymph, and, after genetic analysis, were named as a new species, *R. henselae*. Then, Koehler and coworkers succeeded in isolating *R. henselae* from the cutaneous lesions of patients with BA.

Recently, the genus Rochalimaea was united with Bartonella, and *Rochalimaea henselae* is now reclassified as *Bartonella henselae*.

An indirect fluorescence antibody (IFA) technique was developed to detect *B. henselae* antibodies. Used initially on serum samples from both HIV-infected BA patients and HIV-infected controls, several BA patients showed high-titre antibodies, but only one HIV-infected control gave a strong reaction. Perhaps it was fortuitous that this patient had CSD.

Subsequently, Rennery and coworkers used this IFA test on 41 patients suspected of having CSD, and 36 (88%) had serum titres to *B. henselae* antigen of >1 in 64. Furthermore, there was only a low prevalence (3%) of significant titres in healthy controls. Interestingly, when the sera was tested against *A. felis*, very few samples gave significant titres.

Anderson and coworkers confirmed the association between *B. henselae* and CSD by PCR amplification of *B. henselae* DNA from the antigen used for skin testing. Bergmans and coworkers compared PCR detection of *B. henselae* and *A. felis* DNA with serology and skin tests. They could not detect *A. felis* DNA in clinical samples, and concluded that CSD is caused by *bartonellae*.

Given the body of evidence, it would appear that *B. henselae* is the primary cause of CSD, rather than *A. felis*. However, Alkan and coworkers amplified the 16S rRNA gene from lymph node sections in 12 patients with histological features of CSD, and detected *B. henselae* in five, *A. felis* in three, and both organisms in two. Giladi
A. felis in CSD, after isolating the organism from a lymph node of a patient with CSD. Although they were unable to detect A. felis DNA from 32 B. henselae DNA-positive patients with CSD, they felt that A. felis might play a role in its pathogenesis. La Scola and Raoult$^{36}$ isolated A. felis from a hospital water supply, and suggested that previous isolation of A. felis from lymph nodes may have been due to contamination.

In 1997, a newly described organism, B. clarridgeiae, was recognized as causing CSD in a veterinarian.$^6$ A Bartonella-like organism was isolated from the patient’s cat, and the patient’s sera did not react against B. henselae, B. quintana, or B. elizabethae, but did react (titre: 1 in 24) against the cat isolate. The following year, Margileth and Baehren$^{31}$ described another adult patient with a chest-wall abscess due to CSD, and antibodies to B. clarridgeiae.

**Animal reservoir**

Although the association of CSD with cats is an obvious one, given the name of the syndrome, it was only proven conclusively in the 1990s. In 1992, Regnery and coworkers$^{32}$ isolated B. henselae from an asymptomatic cat on two occasions, and suggested that the domestic cat (Felis domesticus) may be a reservoir for human Bartonella disease.

Zangwill and coworkers$^{33}$ compared CSD patients with age-matched, cat-owning subjects, and found that CSD patients were more likely to own a kitten, been scratched or bitten by a kitten, and to have at least one kitten infested with fleas. Furthermore, serological tests demonstrated that 39 of 48 (81%) patients’ cats had antibodies to B. henselae, compared with 11 of 29 (38%) control cats.

Sander and coworkers$^{34}$ investigated blood cultures from 100 household cats, and isolated B. henselae from 13%. They found that positive cultures were more likely to be found in young female cats (<24 months) than in male and older cats.

Koehler and coworkers$^{35}$ studied cats in the San Francisco area and confirmed the domestic cat to be a large asymptomatic reservoir for human B. henselae infection. The organism was cultured from 25 of 61 (41%) pet and impounded cats, and was found in seven cats belonging to four patients with BA. In addition, B. henselae DNA was detected by PCR in a single flea, and was isolated from Ctenocephalides felis infesting a culture-positive cat. Interestingly, B. henselae could not be isolated from the fleas of a culture-negative cat.

It has been suggested that contamination of cat nails with B. henselae may occur following excoriation of skin during scratching; or periodontal disease may result in saliva becoming contaminated.$^{36}$ As arthropod vectors are responsible for transmitting other members of the genus (i.e., B. quintana by the human body louse, and B. bacilliformis by the sandfly), it would seem plausible that they may be involved in the transmission of B. henselae.$^{36}$

Chomel and coworkers$^{37}$ provided experimental evidence that cat fleas can transmit B. henselae from one animal to another. Fleas removed from cats that were bacteremic with B. henselae transmitted the organism to five specific-pathogen-free kittens in two separate experiments, and all developed B. henselae bacteremia. As the cat flea consumes an average amount of 13.6 μL blood a day, which may contain millions of B. henselae organisms per mL, they considered the potential for ingesting large numbers of organisms to be substantial.

Some fleas can infect mammalian hosts with Bartonella spp. via infected feces. As large amounts of potentially infective flea feces are present in the fur of infested cats, direct inoculation during scratching may lead to feline infection, and be passed directly to humans via claws contaminated with flea feces.$^{37}$ They concluded that the cat flea plays a substantial indirect role in human disease by amplifying the size of the cat reservoir. Although epidemiological data do not support transmission from cat to human via the cat flea, the potential exists.

Whether or not other animals can act as a reservoir for B. henselae is unknown. However, two cases of CSD associated with a dog scratch have been described; one in a nine-year-old boy presenting with osteomyelitis,$^{38}$ the other in a ten-year-old boy with bilateral cervical lymphadenopathy.$^{39}$ In both cases, the only animal contact was with a dog; however, in the second case, Bartonella DNA was found in the gingiva and buccal membrane of the puppy. Tsukahara and coworkers$^{39}$ using IFA, detected significant B. henselae antibody titres in four out of 52 dogs (three titres were 1 in 64, and one was 1 in 128).

**Epidemiology**

CSD has a worldwide distribution, having been reported in the United States,$^{2,25,26,31,40-42}$ Europe (Germany,$^{43-46}$ The Netherlands,$^{27,28}$ Switzerland,$^{51,52}$ France,$^{53,54}$ Spain,$^{55}$ Italy$^{56}$ and the UK$^{57,58}$), Japan,$^{59}$ Israel$^{29,30,59}$ and Australia.$^{60-62}$ In the UK, very few cases were reported after the late 1970s, and this can be attributed directly to the withdrawal of the skin antigen test because of concerns about its safety. However, Harrison and Doshi$^{63}$ measured Bartonella antibodies, and
found that infection is common in the UK, with serological evidence present in 20% of their probable CSD group.

In temperate climates, a higher rate of CSD cases has been reported in the autumn and winter months. Some authors suggest that this may be explained by the seasonal breeding of the domestic cat, which governs when kittens are available to new owners. 2,16

Bass and coworkers 8 considered many variables that might affect the prevalence of CSD, including geographical location, climate and season, and cat-associated variables such as density, age, exposure, and degree of flea infestation. Serological studies in the USA found an increase in B. henselae antibodies in both humans and cats in warm, humid areas, compared with those in the rest of the country. 9

Jackson and coworkers 4 analyzed three national databases in the USA, and found CSD to be an important cause of morbidity, especially in children, where it accounted for more than 15% of lymph-node biopsies performed. CSD was the diagnosis in 0.77-0.86 per 100,000 hospital discharges, and the incidence in ambulatory patients was higher, at 9.3 per 100,000 population. There are an estimated 57 million pet cats in the USA; therefore, the B. henselae reservoir is large and the potential for human infection immense. 31

Clinical presentation

Typically, a non-tender papule 0.5-1 cm in diameter develops in the scratch line, three to ten days after exposure, usually healing without scarring in 2 to 3 weeks. Regional lymphadenopathy follows in more than 80% of cases, but resolves usually within 2 to 3 months. In about 10% of cases, the lymph nodes may suppurate and become fluctuant. In un-complicated CSD, patients usually remain afebrile and do not appear to be ill.

Nowadays, atypical CSD symptoms are seen in up to 25% of cases, which is considerably more than reported previously; however, this increase probably is associated with increased clinical awareness, and it is suggested that these atypical presentations are manifestations of Bartonella infection rather than CSD. Nevertheless, many authors continue to refer to such infection as atypical CSD, presumably because of an association with a scratch or bite. 3,16,64

One of the most common atypical manifestations of CSD is ocular involvement, either via direct inoculation or after rubbing the eye following contact with a cat. Parinaud’s ocuglandular syndrome is a type of conjunctivitis described in up to 6% of patients with CSD. Other ophthalmic manifestations include retinitis, panuveitis, subacute orbital abscess, choriditis, optic nerve masses, branch retinal artery occlusion, and peripapillary angiomata. Most ocular symptoms resolve with or without treatment within 4 months, but severe and permanent vision loss has been reported.

Neurological involvement occurs in a small proportion (1-7%) of cases, usually characterized by encephalopathy. It presents often as the sudden onset of a seizure or coma that may last for several days, but usually resolves with rapid recovery. However, Noyola and coworkers described a CSD patient with recurrent encephalopathy who had two distinct episodes of seizures. Carithers and Margileth 43 reported a clinical account of 76 patients with neurological complications (encephalopathy: 61; convulsions: 35). Armengol and Hendley 68 described six children who presented with sudden onset of status epilepticus (seizures >30 minutes duration) that were diagnosed with CSD, based on clinical criteria and elevated B. henselae titres. As CSD encephalopathy is usually self-limiting without neurological sequelae, they recommended supportive care rather than specific antimicrobial treatment.

Other reported atypical manifestations include granulomatous hepatitis, 71 hepatosplenic infection, 72,73 endocarditis, 74 paronychia, 75 and osteomyelitis. 30,46,60 CSD may be difficult to diagnose and has been mistaken clinically for lymphogranuloma venereum, 76 lymphopharyngeal cancer with lymph-node metastases, 44 and tuberculosis lymphadenitis. 62 Systemic CSD has been reported in both immunocompetent patients and those infected with HIV. The clinical presentation may differ greatly in immunocompromised patients and may become life-threatening.

Clinical diagnosis

Until fairly recently, the diagnosis of CSD relied on meeting at least three of four criteria: 1) animal contact (usually a cat or kitten), with a scratch or eye lesion; 2) a positive CSD skin test; 3) regional lymphadenopathy that develops 2 weeks after contact; and 4) typical histopathological changes in a lymph node biopsy. However, the skin test antigen is not available commercially and is prepared from a pool of tissue from CSD patients. Consequently, it carries an inherent safety risk and may be capable of transmitting pathogens. In addition, it has been reported to be less sensitive and less specific than other diagnostic methods, and, as such, is no longer recommended by some workers.

Laboratory diagnosis

B. henselae can be seen in stained sections of
lymph node (i.e., using Warthin-Starry silver stain or Brown Hopp's Grain stain). As biopsy of the lymph node is an invasive procedure, it should not be used in routine cases but reserved for atypical CSD. The organisms are best observed early in the illness, and may be very difficult to see once the lymph node suppurates.

Although *B. henselae* is fastidious and difficult to grow routinely, it has been isolated successfully from human lymph node tissue, cutaneous BA lesions, and from blood. This is unlikely to be undertaken in a routine diagnostic laboratory, and has only been performed in a handful of laboratories worldwide. Growth is slow, especially on blood agar, and isolates require 5 to 15 days incubation in CO₂. Colonies of *B. henselae* are firm, adherent, often embedded in the agar, and have been described as "cauliflower-like." *B. henselae* are small, curved gram-negative bacilli, with morphology similar to *Campylobacter* spp.

Isolation from human blood may be difficult because *B. henselae* does not produce detectable CO₂ in some blood culture systems. Tierno and coworkers isolated *B. henselae* from the blood of five febrile immunocompromised patients, using the automated BacT/Alert™ system (Organon Teknika, Durham, NC); however, they found it more difficult to isolate from CSD patients.

Gram staining of blood culture specimens often fails to detect *Bartonella* spp; therefore, it is recommended that acridine orange be used to stain blood cultures before discarding them as negative. Brenner and coworkers examined the effect of different methods of blood collection and handling on the isolation of *B. henselae*. Using blood specimens from *B. henselae*-infected cats, they found that freezing and thawing the sample yielded the largest number of colonies, and concluded that cell lysis, disruption of cell membranes, and dispersal of bacterial aggregates improved the sensitivity of *B. henselae* culture from blood.

*B. henselae* are catalase- and oxidase-negative, and display twitching motility; they are non-reactive in routine biochemical tests, and are neither hemolytic nor acid-fast. Cellular fatty acid analysis reveals the major fatty acids to be octadecanoic acid (C₁₈:0, 56%), octadecanoic acid (C₁₈:1ω9c, 25%), and hexadecanoic acid (C₁₆:0, 13%). Such specialized methodology is beyond the scope of most clinical microbiology laboratories; however, Welch and coworkers compared the ability of six commercial identification systems to distinguish *B. henselae* and *B. quintana*, and found that the MicroScan Rapid Anaerobe Panel™ (Baxter Diagnostics, Deerfield, IL) could separate the two, and identify *B. henselae* successfully.

The most common laboratory method used to diagnose CSD is serological detection of *B. henselae* antibodies. In 1992, Regnery and coworkers developed the IFA test for the detection of *B. henselae* antibodies in humans. The antigen was prepared from *B. henselae* co-cultivated with vero cells to reduce the autoadherent nature of the organism. Other workers used an enzyme immunoassay (EIA) to detect IgG, IgM and IgA antibodies in patients with suspected CSD. Barka and coworkers found the EIA method to be highly specific and more sensitive (95%) than the IFA method.

Bergmans and coworkers evaluated both methods of detecting *B. henselae* antibodies. Setting the specificity of the assays at ≥95% by analyzing serum from blood donors, they found the sensitivities of the IgG assays to be very low. However, by increasing the significant titre to ensure that 95% of healthy donors were negative, they may have introduced some bias. For example, Zbinden and coworkers studied 120 blood donors who were positive for *B. henselae*, and found 11 (9.2%) to have antibody titres >1 in 256.

The presence of *B. henselae* antibodies in healthy individuals may depend on many variables, but it appears to be higher in Europe than in the USA. Bergmans and coworkers found the IgM EIA to have the highest sensitivity (71.4%) in patients fulfilling two or more criteria for CSD, and 80.6% in patients with a positive Bartonella PCR result. Furthermore, they recommended that if only IgG IFA is performed, two-point serology is necessary to detect a developing *B. henselae* infection.

Drancourt and coworkers described genotypic variation among *B. henselae* strains and described a separate serogroup (Marseille). Given the inconsistency of serological results in CSD, they suggest that this antigenic variability is partly to blame. Mainardi and coworkers reported CSD due to *B. henselae* serotype Marseille in a seronegative patient, emphasizing the need to incorporate this serotype into future immunofluorescence assays.

Anderson and coworkers characterized a 17-kDa *B. henselae* antigen that provoked a strong antibody response in CSD patients. Using recombinant DNA techniques, they isolated clones that expressed this antigen, and this may prove useful in the development of a simpler serological test. In addition, if the antigen elicits a protective immune response, it may be useful in the development of a suitable vaccine.

PCR techniques have been used to detect *B. henselae*. *Bartonella* spp. are very similar, both
genotypically and phenotypically, and molecular techniques are powerful tools for definitive species identification.\(^4\) In addition, these techniques have been used to good effect in elucidating the etiology of CSD. For example, Bergmans and coworkers\(^2\) used PCR to detect *B. henselae* DNA in pus and lymph node specimens from CSD patients, but failed to detect *A. felis* DNA.

Many different molecular techniques have been employed successfully, including amplification of Bartonella DNA and dot-blot hybridization with a specific *B. henselae* probe,\(^4\) and amplification of *B. henselae* genes encoding for citrate synthase or a 60kDa heat-shock protein.\(^5,\!^6\) Bergmans and coworkers recommended at least two different primer pairs for higher sensitivity, as false-negative reactions are likely when performing PCR for *B. henselae* on fixed and paraffin-wax-embedded tissue.

Molecular methods proved invaluable when typing strains of *B. henselae*, with many authors reporting at least two genotypes.\(^3,\!^4,\!^6,\!^8,\!^9\) It would appear that some *B. henselae* genotypes are more prevalent in different geographical locations. Furthermore, different genotypes were found in cats and humans, which may be related to pathogenicity.\(^9\) Sander and coworkers\(^3\) compared different DNA fingerprinting methods for molecular typing of *B. henselae* and found that genetic heterogeneity was high. This may prove useful in future epidemiological studies.

**Treatment**

The majority of CSD cases resolve spontaneously within a month or two and do not require antibiotic treatment. Zangwill\(^8\) commented on the lack of controlled studies performed to date and regarded much of the information on CSD treatment to be anecdotal. He recommended therapy only in patients with unresolved lymphadenopathy, where lymphadenopathy is associated with significant morbidity, severe systemic disease, or an underlying medical disorder complicated by severe CSD.

Margileth\(^1\) retrospectively reviewed antibiotic therapy for CSD and described 202 patients, in whom 18 different antimicrobial agents were used, only four of which (rifampicin [87% effective], ciprofloxacin [84%], gentamicin [73%], and trimethoprim-sulphamethoxazole [58%]) proved effective. Ciprofloxacin has been used successfully to treat five adult patients with CSD, but is contraindicated in both children and pregnant women.\(^9\)

*B. henselae* is sensitive to many antibiotics when tested on agar, with minimum inhibitory concentration (MIC) \(<\!0.125\ mg/L\ for\ gentamicin,\ tetracycline,\ doxycycline,\ minocycline,\ azithromycin,\ clarithromycin,\ amoxycillin,\ cefotaxime,\ ceftriaxone\ and\ rifampicin.\(^8\) However, these antibiotics are less effective when used clinically, as treatment failure and relapse are common. *B. henselae* is intracellular and therefore MIC testing should be performed in a tissue culture system, where antibiotics have to penetrate the cells.

Musso and coworkers\(^9\) used a cell-line assay to test *B. henselae* against various antimicrobial agents, and found that only aminoglycosides were bactericidal. Ives and coworkers\(^9\) also used a cell-line assay (vero) to evaluate in vitro susceptibilities of *B. henselae* against macrolide antibiotics. They measured the ability of the antibiotics to inhibit rather than eliminate *B. henselae*, and concluded that clarithromycin, roxithromycin and azithromycin may be useful in the treatment of CSD.

Margileth and Baehren\(^1\) considered the treatment of a healthy patient with typical CSD to be supportive. In patients with thoracic or pulmonary disease associated with prolonged symptoms and/or severe multisystem disease, they recommended oral trimethoprim-sulphamethoxazole, ciprofloxacin, or azithromycin. Rifampicin was suggested as an alternative, with gentamicin reserved for the severely ill patient.

In 1998, Bass and coworkers\(^8\) published a prospective, randomized, double-blind placebo-controlled study of the use of azithromycin in CSD. They concluded that patients with typical CSD showed significant clinical benefit after a 5-day course, indicated by a decrease in lymph-node volume within the first month of treatment. However, Zangwill\(^8\) was critical of this study because 10% patients, who had not undergone serological testing, were excluded from the final analysis; and considered a combination of therapeutic restraint and reassurance to be the key with patients presenting with uncomplicated CSD.

Antibiotic treatment is recommended in immunocompromised patients with CSD. Patients with BA, bacillary peliosis hepatis, or relapsing bacteremia should be treated with macrolides or tetracycline, preferably for 6 weeks.\(^8\) Acquired immune deficiency syndrome (AIDS) patients with BA respond dramatically to various antibiotics,\(^2\) and HIV-infected patients require at least 6 to 8 weeks treatment. In immunocompromised patients who relapse, treatment should be continued for 4 to 6 months, and repeated relapses should be treated indefinitely.\(^9\)

**Conclusions**

Cat-scratch disease is a fairly common clinical syndrome that has puzzled microbiologists
for many years. There is now little doubt that B. henselae causes CSD, and is transmitted to man via infected cats; however, in some CSD patients the organism cannot be detected, even by sensitive molecular techniques. This raises the possibility that more than one causative agent is involved.

*A. felis* has been isolated from the lymph nodes of CSD patients, and could be responsible for a small number of cases; however, the lack of a serological response to this organism in humans, and its absence from cats, would seem to argue against this hypothesis.

Genotypic variation among *B. henselae* isolates may result in negative diagnostic tests in CSD patients, especially as the Marseilles serogroup is not screened for routinely. In addition, other *Bartonella* spp., such as *B. clarridgeiae*, also may be associated with CSD.

At the beginning of the 21st century we have a much better understanding of the etiology and epidemiology of CSD; however, there is much still to discover, and the vexing question of how the organism is transmitted from the blood of an asymptomatic cat to man largely remains unanswered.

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References


Questions for STEP Participants

Answer questions only on the official STEP answer sheet. If you do not have the official STEP answer sheet, a year’s supply can be obtained (at no cost) simply by writing to: STEP Program Answer Sheets, American Medical Technologists, 710 Higgins Road, Park Ridge, IL 60068-5765.

In addition to marking your answers, be sure to include all the required information on the answer sheet and a processing fee of $2.00 per article. In the following, choose the one best answer for each question.

1. Cat scratch disease (CSD) was first described in 1864. (True or false.)

2. The etiological agent for CSD eluded detection until 1983. (True or false.)

3. The disorder is so named because it is associated with a cat bite or scratch. (True or false.)

4. Nearly 25% of the 24,000 cases annually require hospitalization. (True or false.)

5. Typically a papule develops in the scratch line in about:
   A. 3 to 5 days
   B. 3 to 7 days
   C. 3 to 10 days
   D. 3 to 15 days

6. The most common laboratory method used to diagnose CSD is serological detection of B. henselae antibodies. (True or false.)

7. One of the criteria for diagnosis of CSD is regional lymphadenopathy, which develops 3 days after contact. (True or false.)

8. The majority of CSD cases:
   A. resolve spontaneously
   B. require intensive treatment
   C. require antibiotic therapy
   D. are in temperate climates

9. Because there are over 57 million cats in the United States, there is an immense reservoir for potential infections. (True or false.)

10. CSD in immunocompromised patients may be life-threatening. (True or false.)