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# Cat-Scratch Disease

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Author Disclosure  
Dr English did not disclose any financial relationships relevant to this article.

**Objectives** After completing this article, readers should be able to:

1. Describe the etiology and epidemiology of cat-scratch disease.
2. Recognize the clinical presentation of cat-scratch disease in immunocompetent patients, including chronic lymphadenopathy and numerous atypical manifestations.
3. Know the various laboratory tests that can aid in the diagnosis of cat-scratch disease.
4. Discuss the therapies that may be useful in the management of cat-scratch disease, realizing that the disease generally is a self-limited infection that resolves without antibiotics.
5. Know the conditions that immunocompromised patients can develop after infection with *Bartonella henselae* or *B quintana*.

## Introduction

Cat-scratch disease (CSD) is a common infection in children. Immunocompetent children who are affected typically have a self-limited course, but immunocompromised patients can develop serious systemic disease following infection. Although antibiotic treatment often is prescribed, very little evidence of its effectiveness in controlled trials has been published in the literature. The most common clinical feature of CSD is regional lymphadenopathy, but reports of other clinical manifestations associated with this infection are increasing.

## Case Study

*A 7-year-old boy presents in January with a daily fever to 103°F (39.5°C) for 3 weeks. He initially complained of sore throat and diffuse abdominal pain followed by right hip, right leg, and back pain. During this illness, he had received brief courses of amoxicillin-clavulanate and azithromycin without relief of symptoms. His past medical history is noncontributory. He has one cat at home.*

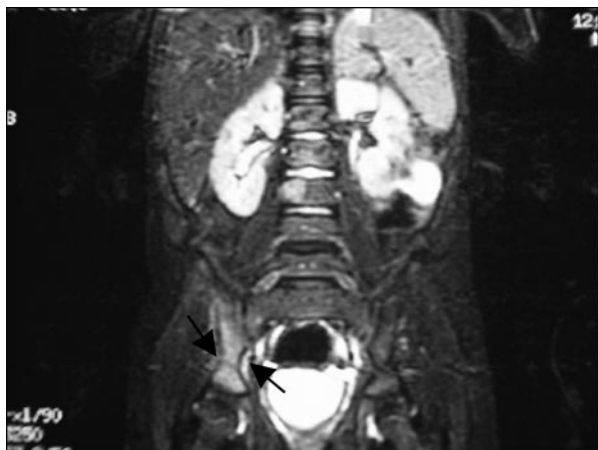
*His physical examination findings are within normal limits. He has no tenderness of the extremities or back and no lymphadenopathy. A complete blood count, purified protein derivative skin test, lactate dehydrogenase level, and uric acid value are normal. The erythrocyte sedimentation rate is 95 mm/hr, and the C-reactive protein is 2.7 mg/L. A bone scan shows increased uptake in the right eighth rib, the right ilium, and the T9 vertebral body.*

*He is hospitalized with a diagnosis of suspected multifocal osteomyelitis. Intravenous oxacillin is initiated, and orthopedics and oncology are consulted. Magnetic resonance imaging (MRI) reveals inflammatory lesions of the T10 and L1 to L3 vertebrae, a lesion in the right supra-acetabular area, and a normal liver and spleen (Fig. 1). A bone marrow biopsy shows no abnormal cells. A bone biopsy of the ilial lesion reveals chronic inflammation with focal microabscesses and a palisade of histiocytes, but examination using Warthin-Starry Silver stain is negative. The boy is diagnosed with presumed cat-scratch osteomyelitis, and a 14-day course of azithromycin and rifampin is started. Bartonella henselae titers obtained at admission subsequently show an immunoglobulin (Ig)G of 1:512, which confirms the diagnosis. He is discharged from the hospital and recovers without sequelae.*

## Etiology and Epidemiology

Initial studies into the cause of CSD suggested *Afipia felis* as the causative organism. However, subsequent studies have shown that *B henselae*, formerly known as *Rochalimaea*

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**Figure 1.** T2-weighted MRI coronal image with fat suppression showing multiple hyperintense foci of abnormal marrow signal in the T10, L1, L2, and L3 vertebrae and right supra-acetabular region (arrow).

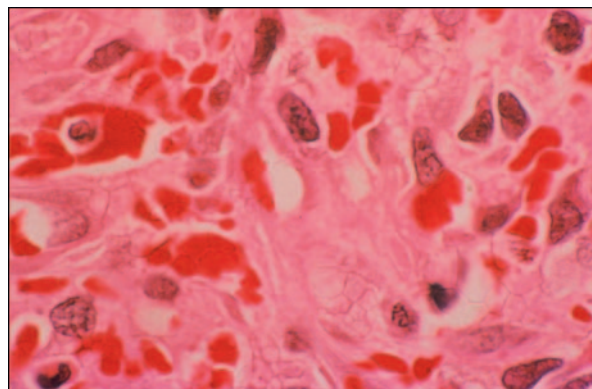
*henselae*, is the organism associated with the clinical syndrome of CSD. *B henselae* and its related species, *B quintana*, *B bacilliformis*, and *B elizabethae*, are fastidious, pleomorphic gram-negative bacilli.

CSD is more common in autumn and winter months and is seen more often in warm, humid climates. The areas of highest prevalence of the clinical disease correlate with areas that have the highest prevalence of *B henselae* antibody in the cat population. Cats younger than 1 year of age have been shown to have a higher rate of both *B henselae* bacteremia and antibody to *B henselae*, and one study found that stray cats had a higher rate of both bacteremia and elevated antibody levels than did pet cats. The transmission of *B henselae* between cats occurs via the cat flea *Ctenocephalides felis*, but this flea is not believed to be responsible for the transmission from cats to humans. Human-to-human transmission does not occur.

Most people who have CSD report contact with cats, especially kittens, but many do not recall an actual scratch or bite. For the typical presentation that includes a history of a previous scratch, the incubation period is 7 to 12 days from the time of the scratch to the development of the skin lesion, and regional lymphadenopathy occurs 1 to several weeks later.

### Pathogenesis

Early in the clinical course of CSD in immunocompetent persons, histologic examination of skin lesions and lymph nodes reveals lymphoid hyperplasia and arteriolar proliferation. Granulomas with occasional multinucle-



**Figure 2.** Skin biopsy showing lobular capillary proliferation in an immunocompromised patient who has bacillary angiomatosis. Obtained with permission from Russell W. Steele, MD.

ated giant cells appear later, and as these granulomas coalesce, necrosis and infiltrating neutrophils cause the formation of stellate microabscesses. These findings also may be seen in biopsies of patients who have lymphogranuloma venereum, tuberculosis, and tularemia, but the concurrent presence of granulomas and microabscesses suggests CSD.

Another histologic characteristic that helps to distinguish CSD from other infections is the visualization of bacilli by using the Warthin-Starry silver stain, but the absence of the bacilli when using this technique does not exclude the diagnosis. This stain does not differentiate between *B henselae* and other *Bartonella* sp. If bacilli are seen, they are noted in blood vessel walls, in red blood cells, and within areas of necrosis.

In immunocompromised patients who have bacillary angiomatosis, the histologic features are somewhat different, with vascular proliferation and neutrophilic infiltration being more common than granuloma and stellate microabscess formation (Fig. 2).

### Clinical Aspects

CSD is one of the most common causes of chronic lymphadenitis in children. The typical presentation begins with a scratch or bite from a cat, followed by the development of a brownish-red papule at the site of contact 7 to 12 days later. Lymphadenopathy, often in regional sites draining the area of the papule, occurs 1 to several weeks later. Cervical and axillary lymphadenopathy are most common, but submandibular, preauricular, femoral, and inguinal nodes also have been affected. Affected lymph nodes may be very small and undetected or they may enlarge to several centimeters. The nodes often are tender, warm, and erythematous, and 10% to

30% eventually suppurate. Enlarged nodes may persist for weeks to months.

Fever, with temperatures as high as 104°F (40°C), has been described in 30% to 50% of patients. Other constitutional symptoms, such as malaise, anorexia, rash, and sore throat, are less common. Patients usually appear to be well. Other infections that can cause a similar presentation are those caused by atypical mycobacteria, tularemia, brucellosis, toxoplasmosis, and tuberculosis. Malignancy, specifically lymphoma and leukemia, and sarcoidosis also are in the differential diagnosis and should be considered in patients who have chronic lymphadenopathy.

Atypical presentations of CSD have been described more frequently in the last few years, with recent studies showing that 20% to 25% of cases come to medical attention for reasons other than lymphadenopathy. One of the more common atypical manifestations of CSD infection is Parinaud oculoglandular syndrome, which also can occur with other infections, such as tularemia, tuberculosis, and syphilis. In oculoglandular syndrome, the site of inoculation is the conjunctiva, and the ensuing lymphadenopathy is in the preauricular and, less commonly, submandibular areas. The conjunctivitis typically is nonsuppurative and painless, with a conjunctival granuloma at the inoculation site.

Prolonged fever of unknown origin (FUO) without lymphadenopathy is the presenting symptom in 10% to 30% of cases of CSD; a recent study of 146 patients presenting with FUO found that approximately 5% had CSD. Multifocal hepatosplenic microabscesses and osteolytic bone lesions have been described in many patients, both those who had and those who did not have fever or other features of CSD. Thrombocytopenic purpura associated with CSD has been reported rarely.

Neurologic complications of CSD have been well described in the literature, ranging from headache and cranial or peripheral nerve abnormalities to encephalopathy with mental status changes and seizures. A recent review of five previously healthy school-age children who had status epilepticus found that four evidenced CSD on serology. Neuroretinitis and transverse myelitis also have been reported.

In the last few years, a number of case reports have associated CSD with other disease processes. A review of patients who had Henoch-Schönlein purpura found a significant increase in antibody titers to *B henselae* compared with controls, suggesting an association of previous CSD infection with the development of Henoch-Schönlein purpura. The development of systemic bartonellosis has been reported in association with



**Figure 3.** Typical appearance of skin lesions in a patient who has bacillary angiomatosis. Obtained with permission from Russell W. Steele, MD.

Epstein-Barr virus coinfection. One patient presented with ileitis and was found to have CSD rather than inflammatory bowel disease. Cases of acute renal transplant rejection due to CSD have been reported. Therefore, it is apparent that atypical presentations of CSD are being recognized more commonly, and clinicians should be aware of these different manifestations.

### The Immunocompromised Host

*Bartonella* infections can present differently in patients who are immunocompromised, especially those who have AIDS. Bacillary angiomatosis and bacillary peliosis are the clinical syndromes seen in these patients and may be caused either by *B henselae* or, less commonly, by *B quintana*. Bacillary angiomatosis, or epithelioid angiomatosis, is characterized by nontender, firm, red-to-purple or skin-colored lesions, which may vary from a few millimeters to a few centimeters in size (Figs. 3 and 4.) Lesions may be papular or nodular and can be indistinguishable from pyogenic granuloma, Kaposi sarcoma, or some types of hemangioma. If antibiotic treatment is not initiated, dissemination to multiple organs is probable, which may be accompanied by numerous constitutional symptoms, such as fever, weight loss, and nausea.

Bacillary peliosis is a systemic condition characterized by vasoproliferation within the liver and spleen and occasional involvement of abdominal lymph nodes and bone marrow. This condition may be present with or without evidence of bacillary angiomatosis and may be seen in malignancies or other immunodeficiency states. Histologic features of peliosis include blood-filled cysts, which may be surrounded by fibrosis, and bacilli may be identified in the cysts.





**Figure 4.** Typical appearance of a skin lesion in an adult patient who has bacillary angiomatosis. Obtained with permission from Russell W. Steele, MD.

## Diagnosis

For patients who are suspected of having CSD, serologic testing by using enzyme immunoassay (EIA) or the immunofluorescent antibody (IFA) test is useful to confirm the diagnosis. The IFA test can be obtained from the Centers for Disease Control and Prevention; tests obtained from commercial laboratories may not be as reliable. IFA assay for *B henselae* IgG has been studied extensively and has been shown to have a sensitivity of 88% to 100% and a specificity of 92% to 98%. A recent study of EIA, which accepted positive anti-*B henselae* IgM or IgG as being diagnostic, showed a sensitivity of 85% and a specificity of 98% to 99%.

Wide variability in the timing of positivity of both IgM and IgG in relation to the clinical course of CSD has been demonstrated. Some patients demonstrate low antibody production and some produce high levels of either one or both classes of antibodies. A recent study that examined the EIA results in 98 patients who had CSD showed that only 53% were positive for IgM; 92% of these were negative after 3 months. Positive IgG antibodies were found in 92% of patients; 25% of these remained positive after 24 months. Cross-reaction with anti-*B quintana* antibodies can occur with both EIA and IFA methods for *B henselae*.

DNA polymerase chain reaction (PCR) assays are less widely available than IFA and EIA, but they have been shown to be sensitive for the diagnosis of CSD. The organism can be cultured from affected lymph nodes, although this technique requires an incubation period of up to 6 weeks and, therefore, may not be practical. An antigen skin test created from the pus of CSD-infected lymph nodes was used in the past for diagnosis but no longer is recommended because of the risk of transmis-

sion of other infections and because it was not standardized. Sensitive and specific serologic tests have supplanted the need for the skin test.

Occasionally, lymph node biopsy or histologic examination of other tissues is necessary to confirm the diagnosis of CSD, but these usually are reserved for cases that have atypical findings or if the diagnosis remains in question after serologic testing. Radiologic tests, such as MRI or computed tomography scan, may show positive findings such as microabscesses in the liver and spleen or lytic bone lesions, but these are not pathognomonic and should only be used to determine the extent of disease and to identify potential sites for biopsy.

## Management

CSD in immunocompetent persons generally is self-limited and requires supportive care in most patients, including warm compresses to affected nodes and antipyretics. Many studies of antibiotic treatment have shown little or no improvement. Antibiotics that have shown the highest activity against *B henselae* in both in vitro and clinical studies are the macrolides, rifampin, doxycycline, ciprofloxacin, and gentamicin.

Most evidence regarding antimicrobial therapy is based on case studies or retrospective reviews. A retrospective review of 202 patients published more than 10 years ago found that of 18 antibiotics used to treat typical and atypical CSD, only rifampin, ciprofloxacin, gentamicin, and trimethoprim-sulfamethoxazole (TMP-SMX) were effective. Another recent retrospective review of 19 cases of hepatosplenic CSD found favorable clinical responses (time to defervescence) with rifampin, either alone or in combination with gentamicin or TMP-SMX. A few case studies have suggested an improvement in lymph node size with azithromycin treatment. The only prospective, randomized, placebo-controlled study of antibiotic therapy to date was published in 1998. This double-blind evaluation of 29 patients who had typical CSD showed a decrease in lymph node size in the first 30 days of illness in patients treated with azithromycin compared with placebo, but no difference after 30 days. More randomized, prospective studies are needed to determine the benefit that antibiotics afford. Despite a lack of evidence from controlled trials that antibiotic treatment is indicated in CSD, patients who have severe or disseminated disease may recover more quickly with antibiotics. Thus, their use should be strongly considered in these cases.

Unlike immunocompetent patients who have CSD, who may be observed with supportive management only, immunocompromised patients who have bacillary angio-

omatosis or bacillary peliosis should be treated with antibiotics. Erythromycin or doxycycline, alone or in combination with gentamicin or rifampin, should be used. Treatment with antibiotics often results in significant improvement, which may be either immediate or slow to occur. Relapses may occur, and prolonged treatment with antibiotics may be necessary.

Suppurative lymph nodes may be treated with needle aspiration, which may decrease pain and provide material for diagnosis, but incision and drainage is not recommended because of the risk of prolonged drainage and sinus tract formation. Surgical excision usually is unnecessary and should be reserved for cases in which the diagnosis is uncertain or the course is very atypical or prolonged.

Several case reports have suggested an improvement in CSD symptoms after the initiation of corticosteroids, specifically in a few patients who had eye involvement, encephalopathy, and hepatosplenic disease and had not improved with antibiotic therapy. Further studies are needed to examine the role that corticosteroids may play in the management of this disease.

### Prevention and Prognosis

The best prevention for CSD is elimination of fleas, which decreases transmission among cats. Declawing cats also may be helpful. Removal of the cat from the home is not necessary, but careful play with the cat can be recommended to decrease the incidence of bites or scratches. In the case of hospitalization, standard precautions only are recommended.

CSD carries an excellent prognosis regardless of clinical presentation and antibiotic therapy. Supportive care

and reassurance about the benign nature of the illness are usually all that is required in management. Most cases resolve within 2 to 4 months, but patients should be advised that affected lymph nodes may remain enlarged for several months and, rarely, years. Untreated bacillary angiomatosis in immunocompromised patients can be fatal, but patients who are treated often have a good prognosis.

### Suggested Reading

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## PIR Quiz

Quiz also available online at [www.pedsinreview.org](http://www.pedsinreview.org).

1. Which of the following is a *true* statement regarding cat-scratch disease?
  - A. *Afipia felis* is believed to be the causative organism.
  - B. Elimination of fleas is the best way to avoid cat-scratch disease.
  - C. Human-to-human transmission is the most common mode of transmission.
  - D. Pet cats have a higher incidence of bacteremia than stray cats.
  - E. Removal of the cat from the home is required for full recovery.
2. You are evaluating a 5-year-old girl who has had right anterior cervical lymphadenopathy for 3 weeks. She reports getting a new kitten 2 months ago. Findings on her physical examination are unremarkable except for a 3×3 cm mobile lymph node in the right anterior cervical triangle. You suspect cat-scratch disease. Which of the following is the *most* appropriate initial management of this patient?
  - A. Admit her to the hospital for intravenous gentamicin therapy.
  - B. Observe her on an outpatient basis without medications.
  - C. Perform a needle aspiration of the lymph node.
  - D. Prescribe a 5-day course of oral steroids.
  - E. Refer her to an otolaryngologist for surgical excision of the lymph node.
3. An 8-year-old girl who has a 3-week history of daily fevers to 102°F (40°C) presents to your office for evaluation. She denies other symptoms. She denies any cat scratches but reports that she occasionally plays with a cat behind her house. Overall, she appears well, and her physical examination findings are normal except for a 1×1 cm axillary lymph node on the left. You suspect cat-scratch disease but would like to confirm the diagnosis. Which of the following tests is *most* appropriate at this time?
  - A. *Bartonella henselae* antigen skin test.
  - B. Blood culture for *Bartonella henselae*.
  - C. Immunofluorescent antibody assay for *Bartonella henselae*.
  - D. Lymph node biopsy.
  - E. Magnetic resonance imaging of the liver and spleen.
4. Which of the following statements regarding the management of cat-scratch disease is *true*?
  - A. Antibiotic therapy should be initiated in immunocompromised patients who have evidence of bacillary angiomatosis.
  - B. Bacillary peliosis is a self-limited condition that does not require treatment.
  - C. Corticosteroids have been proven effective in reducing the size of lymph nodes in patients who have cat-scratch disease.
  - D. If antibiotic therapy is to be initiated, a lymph node should be biopsied first to confirm the diagnosis of cat-scratch disease.
  - E. The antibiotic shown to be most effective against cat-scratch disease is amoxicillin-clavulanic acid.

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