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CAT-SCRATCH DISEASE

ALTHOUGH PARINAUD'S 1889 account[1] of a patient with persistent conjunctival inflammation, preauricular adenopathy, enlargement of regional lymph nodes, and low grade fever may have been the first description of cat-scratch disease (CSD), the quest to find an etiologic agent continued for almost a century. In 1988, researchers at the Armed Forces Institute of Pathology (AFIP) announced[2] that they had cultured pleomorphic, slightly curved Gram-negative rods from the lymph nodes of 10 of 19 patients with CSD, but none of 19 controls. Moreover, 3 of 7 patients had ≥4-fold rises in antibody titers to the organism.

The newly described organism was subsequently christened *Afipia felis*, after the AFIP. Not everyone jumped on the *Afipia* bandwagon, however. In 1992, Regnery et al.[3] reported that 88% of 41 patients with CSD, but only 3% of 107 controls had high levels of antibodies to a newly described bacterium, *Bartonella henselae*.* *A. felis* is not closely related to *B. henselae*, and anti-*B. henselae* serum did not cross-react with *A. felis* antigen. *B. henselae* was subsequently cultured from biopsies of CSD patient's lymph nodes,[4] and *B. henselae* DNA sequences were detected in specimens from patients with CSD[5] and even from CSD skin-test antigen.[6] Although *A. felis* has also been isolated from diseased lymph nodes, its role as a pathogen remains unclear. *B. henselae* is now thought to be the principal cause of CSD.

CLINICAL DISEASE

CSD often begins with the appearance at the inoculation site of a 2-3 mm macule that becomes papular within a few days. The papule may persist for several weeks and then resolve. Regional lymphadenopathy may develop, usually within 2 weeks, and may be accompanied by low grade fever, fatigue, and headache. Affected nodes, which may be tender and suppurative, are usually proximal to the site of a scratch or bite. Symptoms usually resolve with no sequelae.[1,7]

Encephalitis complicates a small proportion of cases, typically presenting 2-6 weeks after the initial illness.[8]

Other syndromes

Bacillary angiomatosis is a recently recognized syndrome, probably caused by both *B. henselae* and *B. quintana*, that is seen primarily among immunocompromised persons, notably those with HIV infection.[9] The spectrum of this peculiar vascular disease ranges from a non-specific febrile disease, to serious skin lesions (resembling Kaposi's sarcoma), life-threatening peliosis hepatica, and infection of the liver parenchyma.

B. henselae may occasionally cause fever and bacteremia even in immunocompetent hosts.[10]

OUT OF THE TRENCHES

The taxonomic affinity of these organisms has been in a state of flux. Originally placed in the family Rickettsiaceae, which includes the etiologic agents of typhus, Rocky Mountain spotted fever, tsutsugamushi, and Q fever, among other horrors, more recent analyses suggest that *Bartonella* spp. are not rickettsiae at all, but more closely related to *Brucella* spp. The genus *Rochalimaea* has been subsumed into *Bartonella*.

The aforementioned *B. quintana* (né *Rickettsia quintana*; briefly *Rochalimaea quintana*) is the causative agent of trench fever, a febrile illness of variable severity. Trench fever is spread by body lice, and was common among troops in World War I. Interestingly, *B. quintana* recently turned up in a number of bacteremic Seattle patients with histories of chronic alcoholism and homelessness.[11] Although initial blood cultures appeared negative, acridine-orange staining of the Bactec® culture media revealed organisms that could be subcultured on chocolate agar.

DIAGNOSIS OF CSD

Diagnosis depends on a consistent clinical picture supported by laboratory results, most commonly an indirect fluorescent antibody test that has a reported 84-88% sensitivity and 96-97% specificity.[3,12] Culture is difficult but obviously highly specific. Other methods that have been developed include a PCR assay to identify *B. henselae* in purulent lymph node aspirates.[5]

TREATMENT

Treatment is generally supportive, although excision of affected lymph nodes(s) and the use of antimicrobials may be indicated for treatment of severe swelling, pain, or suppuration. Although antimicrobial agents such as trimethoprim-sulfamethoxazole (TMP/SMX), rifampin, amoxicillin, and tetracycline exhibit in vitro antimicrobial activity against *B. henselae*, antimicrobial therapy has not been consistently beneficial in reducing the duration or severity of CSD. Margileth studied the clinical efficacy of several regimens in patients with prolonged fever, systemic symptoms and/or severe lymphadenitis.[13] Rifampin (10-20 mg/kg/d, in 2-3 doses, maximum dose 600 mg x 7-14 days) was 87% effective. Ciprofloxacin (20-30 mg/kg/d in 2 divided doses x 7-14 days) was 84% effective in patients

CSD and Bacillary Angiomatosis: A Comparison

Variable	*CSD*	*Bacillary Angiomatosis*
Host	immunocompetent	immunocompromised
Cause	*B. henselae* *A. felis?*	*B. henselae*, *B. quintana*
Pathologic Findings	lymphoid hyperplasia, microabscess formation	ectatic capillaries, neutrophilic infiltrate
Usual Presentation	lymphadenopathy	cutaneous lesions, visceral peliosis
Clinical course	self-limited	progressive
Diagnostic tests	serology, histopath, skin test, lymph node culture, 16s RNA analysis	histopath, serology, blood culture, 16s RNA analysis
Antimicrobial Therapy	generally not necessary; rifampin, ciprofloxacin, gentamicin, TMP/SMX	doxycycline, erythromycin

* Most readers will be familiar with the role of that other *Bartonella*, *B. bacilliformis*, in the etiology of Oroya fever, a sand-fly vectored infection found in South America. Crossword puzzle enthusiasts remember Oroya fever as the only known intraerythrocytic bacterial infection.

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>12 years old. Oral TMP/SMX (6-8mg/kg of trimethoprim 2-3 times daily x 7 days) was 58% effective. In the rare severely ill patient, gentamicin sulfate (5mg/kg/d, in divided doses every 8 h IM) was 73% effective, usually within 72 hrs. Oral corticosteroids were not recommended; several patients with neuroretinitis did not respond to steroid therapy.

EPIDEMIOLOGY AND PREVENTION

CSD occurs worldwide, and is now considered the most common cause of unilateral regional lymphadenopathy in children. Persons of all ages and sexes can be infected. In a review of national data, the median age of cases was 15-18; 60% were male.[14] In temperate climates, the disease is most common in the fall and winter. In the United States, an estimated 22,000 cases of CSD occur annually—an incidence of 9.3 per 100,000.[14] (Oregon would have almost 300 cases per year at that rate.) Family clusters have been noted, with cases occurring within a few weeks of each other.

Domestic cats appear to be the most important reservoir for *B. henselae,* although some role for dogs or other animals has not been ruled out. Risk factors for both bacillary angiomatosis and CSD include owning a cat (especially a kitten), being scratched by a cat, and having a cat with fleas.[9,12] About 90% of patients have a history of exposure to cats; 75% report a scratch or bite. The bacteria are usually introduced through traumatized skin and does not require a scratch; direct contact and some compromise of skin integrity is sufficient. Declawing cats has not yet been proven to prevent the disease, but may prevent damage to furniture.

Prevention of CSD depends on eliminating contact between infected cats and humans.* Cats should receive routine veterinary care to prevent or treat ectoparasitic infestations. The potential for *B. henselae* transmission can also be decreased by keeping kittens and other household pets indoors and by not playing roughly with them(!). The public should be educated to avoid contact with stray animals, to disinfect bite and scratch wounds, and to seek appropriate medical care for severe injuries or illness suggestive of CSD.

INFECTION IN ANIMALS

B. henselae is not known to cause disease in cats, and there is no known recommended treatment for infected animals. One paper noted that tetracycline reduced the degree of bacteremia, but the "effectiveness of treatment on preventing reinfection or recrudescence is unknown."[8] Although infected cats develop anti-*Bartonella* antibodies, bacteremia (continuous or intermittent) may persist indefinitely.[15,16] Antibodies were detected in 81% of cats associated with human cases of CSD in Connecticut, compared to 38% of control cats.[12] *B. henselae* was isolated from 41% of blood samples from 61 apparently healthy cats tested in Northern California; fleas from five of these cats were PCR-positive.[15] In another study,[16] 81 (40%) of 205 cats tested were bacteremic. Impounded or stray cats were almost 3 times more likely to be positive. Younger cats (<1 year old) were somewhat more likely to be infected. Over 80% of cats tested had antibodies to *B. henselae.*

* Given the prevalence of *B. henselae* in cats, readers are invited to draw their own conclusions.

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