

60 - 177 Bartonella

Infections, Including Cat-Scratch Disease

177 Bartonella Infections, Including Cat-Scratch Disease

duration of therapy. On the basis of retrospective case series and in vitro sensitivity data, fluoroquinolone therapy is effective for bacteremia in adults; for example, ciprofloxacin is given at a typical dose of 500 mg twice daily by mouth or 400 mg twice daily IV for at least 2 weeks (longer if positive blood cultures persist). A third-generation cephalosporin is an alternative—e.g., cefotaxime (typical dose, 6–8 g/d in 3 or 4 divided doses) or ceftriaxone. In children, third-generation cephalosporins are effective; for example, cefotaxime is given to children ≥ 1 month of age at a typical dose of 75–100 mg/kg per day in 3 or 4 divided doses, with an increase to 150–200 mg/kg per day in severe cases (maximal daily dose, 8–10 g). Amoxicillin and amoxicillin-clavulanate have shown poor efficacy in case series. Trimethoprim-sulfamethoxazole, gentamicin, and imipenem are all active in vitro. *Y. pseudotuberculosis* strains do not express β -lactamase but are intrinsically resistant to polymyxin. Because human infection with *Y. pseudotuberculosis* is less common than that with *Y. enterocolitica*, less case information is available; however, studies in mice suggest that ampicillin is ineffective. Drugs similar to those used against *Y. enterocolitica* should be used. The best results have been obtained with a quinolone.

Some trials of treatment for reactive arthritis (with a large proportion of cases due to *Yersinia*) found that 3 months of oral ciprofloxacin therapy did not affect outcome. One trial in which the same therapy was given specifically for *Y. enterocolitica*-reactive arthritis found that, while outcome indeed was not affected, there was a trend toward faster remission of symptoms in the treated group. Follow-up 4–7 years after initial antibiotic treatment of reactive arthritis (predominantly following *Salmonella* and *Yersinia* infections) demonstrated apparent efficacy in the prevention of chronic arthritis in HLA-B27-positive individuals. A trial showing that azithromycin therapy did not affect outcome in reactive arthritis included cases thought to have followed yersiniosis, although no breakdown of cases was provided. PART 5 Infectious Diseases ■

■ PREVENTION AND CONTROL Current control measures are similar to those used against other enteric pathogens like *Salmonella* and *Campylobacter*, which colonize the intestine of food animals. The focus is on safe handling and processing of food. No vaccine is effective in preventing

intestinal colonization of food animals by enteropathogenic *Yersinia*. Consumption of food made from raw pork (which is popular in Germany and Belgium) should be discouraged at present because it is not possible to eliminate contamination with the enteropathogenic *Yersinia* strains found world wide in pigs. Exposure of infants to raw pig intestine during domestic preparation of chitterlings is inadvisable. Modification of abattoir technique in Scandinavian countries from the 1990s onward included the removal of pig intestines in a closed plastic bag; levels of carcass contamination with *Y. enterocolitica* were reduced, but such contamination was not eliminated. Experimental pig herds free of pathogenic

Y. enterocolitica O:3 (and also of *Salmonella*, *Campylobacter*, *Toxoplasma*, and *Trichinella*) have been established by selective breeding in Norway but remain rare. In the food industry, vigilance is required because of the potential for large outbreaks if small numbers of enteropathogenic yersiniae contaminate any ready-to-eat food whose safe preservation is based on refrigeration before consumption. The rare phenomenon of contamination of blood for transfusion has proved impossible to eradicate. However, leukodepletion is now practiced in most blood transfusion centers, primarily to prevent non hemolytic febrile transfusion reactions and alloimmunization against HLA antigens. This measure reduces but does not eliminate the risk of *Yersinia* blood contamination. Notification of yersiniosis is now obligatory in some countries. ■ ■ FURTHER READING Plague Campbell SB et al: Animal exposure and human plague, United States, 1970–2017. *Emerg Infect Dis* 25:2270, 2019.

Demeure C et al: *Yersinia pestis* and plague: An updated view on evolution, virulence determinants, immune subversion, vaccination and diagnostics. *Microbes Infect* 21:202, 2019. Klunk J et al: Evolution of immune genes is associated with the Black Death. *Nature* 611:312, 2022. Nelson CA et al: Antimicrobial treatment and prophylaxis of plague: Recommendations for naturally acquired infections and bioterrorism response. *MMWR Recomm Rep* 70(No. RR-3):1, 2021. Salam AP et al: Deaths associated with pneumonic plague, 1946–2017. *Emerg Infect Dis* 26: 2432, 2020. World Health Organization: WHO guidelines for plague management: Revised recommendations for the use of rapid diagnostic tests, fluoroquinolones for case management and personal protective equipment for prevention of post-mortem transmission, May 27, 2021. Available at: <https://www.who.int/publications/i/item/9789240015579>. Accessed February 16, 2024. Yang R et al: *Yersinia pestis* and plague: Some knowns and unknowns. *Zoonoses (Burlingt)* 3:5, 2023. Yersiniosis Francis MS et al: The pathogenic *Yersiniae*—advances in the understanding of physiology and virulence. *Front Cell Infect Microbiol* 9:119. 2019. Savin C et al: Genus-wide *Yersinia* core-genome multilocus sequence typing for species identification and strain characterization. *Microb Genom* 5:e000301, 2019. Šumilo D et al: Forgotten but not gone: *Yersinia* infections in England, 1975 to 2020. *Eurosurveillance* 28:2200516, 2023. Michael Giladi, Moshe Ephros

Bartonella Infections,

Including Cat-Scratch

Disease *Bartonella* species are fastidious, facultative intracellular, slow-growing, gram-negative bacteria that cause a broad spectrum of diseases in humans. This genus includes >40 distinct species or subspecies, of which at least 20 have been recognized as confirmed or potential human pathogens; *Bartonella bacilliformis*, *Bartonella quintana*, and *Bartonella henselae* are most

commonly identified (Table 177-1). Most *Bartonella* species have successfully adapted to survival in specific domestic or wild mammals. Prolonged intraerythrocytic and endothelial cell infection in these animals creates a niche where the bacteria are protected from both innate and adaptive immunity and which serves as a reservoir for human infections. Chronic bacteremia, which may persist even following prolonged antimicrobial therapy, is a typical finding in *Bartonella*-hosting mammals. Adhesion and entry to endothelial cells and erythrocytes is facilitated by the *Bartonella* adhesin A or variably expressed outer-membrane proteins. *Bartonella* characteristically evades the host immune system by modification of its virulence factors (e.g., lipopolysaccharides or flagella) and by attenuation of the immune response. Arthropod vectors are often involved. Humans are incidental hosts for most *Bartonella* species with the exception of *B. quintana* and *B. bacilliformis*, which are not considered zoonotic agents. Isolation and characterization of *Bartonella* species are difficult and require special techniques. Clinical presentation generally depends on both the infecting *Bartonella* species and the immune status of the infected individual. *Bartonella* species are susceptible to many antibiotics *in vitro*; however, clinical responses to therapy and studies in animal

TABLE 177-1 <i>Bartonella</i> Species Known or Suspected to Be Human Pathogens	BARTONELLA SPECIES ^a	DISEASE(S) ^b	RESERVOIR HOST(S) ^c	ARTHROPOD VECTOR
	<i>B. alsatica</i>	Endocarditis, lymphadenitis, vascular graft infection		
	<i>B. ancashensis</i>	Verruga peruana, bacteremia	Unknown	
	<i>B. bacilliformis</i>	Carrión's disease	Humans	Sandflies (<i>Lutzomyia verrucarum</i>)
	<i>B. clarridgeiae</i>	Possibly cat-scratch disease	Cats, dogs	Unknown
	<i>B. doshiae</i>	Bacteremia, arthralgia, blurred vision	Voles, rats	Unknown
	<i>B. elizabethae</i>	Endocarditis	Rats, dogs	Fleas
	<i>B. grahamii</i>	Lymphadenopathy, possibly retinitis and retinal vascular occlusion		
	<i>B. henselae</i>	Cat-scratch disease, bacillary angiomatosis, bacillary peliosis, bacteremia, endocarditis		
	<i>B. koehlerae</i>	Endocarditis	Cats	Unknown
	<i>B. kosoyi</i>	Lymphadenopathy	Rats	Fleas
	" <i>Candidatus Bartonella mayotimonensis</i> " ^d	Endocarditis	Bats	Unknown
	" <i>Candidatus Bartonella melophagi</i> " ^d	Various clinical manifestations	Sheep	Sheep keds
	<i>B. quintana</i>	Trench fever, chronic bacteremia, bacillary angiomatosis, endocarditis		
	<i>B. rochalimae</i>	Bacteremia, fever, splenomegaly	Foxes, coyotes, dogs, skunks, rats, other rodents	
	<i>B. schoenbuchensis</i>	Bacteremia, fever, myalgia, deer ked dermatitis?		
	<i>B. tamiae</i>	Bacteremia, fever, myalgia, rash	Rats	Unknown
	<i>B. tribocorum</i>	Bacteremia, myalgia, headache	Rats, mice	Unknown
	<i>B. vinsonii</i> subsp. <i>arupensis</i>	Endocarditis, febrile illness	Mice, dogs	Ticks
	<i>B. vinsonii</i> subsp. <i>berkhoffii</i>	Endocarditis	Domestic dogs, coyotes, gray foxes	Ticks
	" <i>Candidatus Bartonella washoensis</i> " ^d	Endocarditis, myocarditis, meningitis	Squirrels, rabbits, prairie dogs, possibly other rodents	

^aMany other *Bartonella* species exist but are not recognized as human pathogens.

^bAnimal-associated *Bartonella* species (*B. henselae*, *B. doshiae*, *B. schoenbuchensis*, and *B. tribocorum*) were isolated from blood of patients who reported tick bites and chronic symptoms such as fatigue and myalgia. DNA of *B. henselae*, *B. vinsonii* subsp. *berkhoffii*, *B. koehlerae*, or *B. melophagi* or co-infection with more than one *Bartonella* species was detected by polymerase chain reaction in blood samples from patients with extensive arthropod and animal exposure who presented with chronic neurologic or neurocognitive syndromes. The causal relationship between bacteremia with these pathogens, tick bites, and clinical manifestations needs to be established.

^cAnimals are implicated when existing evidence supports their infection with *Bartonella* species. Data supporting animal-to-human transmission may be lacking.

^d*Candidatus* is a taxonomic status for bacteria that cannot be described in sufficient detail to warrant establishment of a novel taxon or cannot be cultured or propagated in culture media. The phylogenetic relatedness of these bacteria has been determined by gene amplification and sequence analysis. models suggest that

the minimal inhibitory concentrations of many antimicrobial agents correlate poorly with the drugs' in vivo efficacies in patients with Bartonella infections.

CAT-SCRATCH DISEASE ■ ■ DEFINITION AND ETIOLOGY

Usually a self-limited illness, cat-scratch disease (CSD) has two general clinical presentations. Typical CSD, the more common, is characterized by subacute regional lymphadenopathy; atypical or extranodal CSD is the collective designation for numerous extranodal manifestations involving various organs. *B. henselae* is the principal etiologic agent of CSD. Rare cases have been associated with *Afipia felis* and other Bartonella species. ■

■ EPIDEMIOLOGY

CSD occurs worldwide, favoring warm and humid climates. In temperate climates, incidence peaks during fall and winter. Adults are affected nearly as frequently as children. Intrafamilial clustering is rare, and person-to-person transmission does not occur. Apparently healthy bacteremic cats constitute the major reservoir of *B. henselae*, and cat fleas (*Ctenocephalides felis*) may be responsible for cat-to-cat transmission. CSD usually follows contact with cats (especially kittens), but other animals (e.g., dogs) have been implicated as possible reservoirs in rare instances. In the United States, the estimated annual disease incidence is 4–9 outpatient cases per 100,000 population with a higher incidence among those who lived in the southern United States and among children 5–9 years of age. About 5–10% of patients in the United States are

Rabbits Fleas Mice, voles, rats, deer Fleas Cats, other felines Cat fleas (*Ctenocephalides felis*): associated with cat-to-cat, but not with cat-to-human, transmission Humans Human body lice (*Pediculus humanus corporis*) Fleas Cattle, roe deer, moose Unknown

CHAPTER 177 Fleas, ticks Bartonella Infections, Including Cat-Scratch Disease

hospitalized. A higher proportion of hospitalization has been reported in Israel. ■ ■ PATHOGENESIS Although cat fleas are likely responsible for cat-to-cat transmission, the mode of cat-to-human transmission is undetermined. *B. henselae*-infected cats' saliva spreads to claws by self-licking, and *B. henselae*-contaminated flea feces can be inoculated by a scratch or a bite. Infection of mucous membranes or conjunctivae via droplets or licking may occur as well. With lymphatic drainage to one or more regional lymph nodes in immunocompetent hosts, a TH1 response can result in necrotizing granulomatous lymphadenitis. Dendritic cells, along with their associated chemokines, play a role in the host inflammatory response and granuloma formation. ■ ■ CLINICAL MANIFESTATIONS AND PROGNOSIS Of patients with CSD, 85–90% have typical disease. The primary lesion, a small (0.3- to 1-cm) painless erythematous papule or pustule, develops at the inoculation site within days to 2 weeks in about one-third to two-thirds of patients (Fig. 177-1A, B). Lymphadenopathy develops 1–3 weeks or longer after cat contact. The affected lymph node(s) are enlarged and usually painful, sometimes have overlying erythema, and suppurate in ~10% of cases (Fig. 177-1C, D, and E). Axillary/epitrochlear nodes are most commonly involved, followed by head/neck nodes and inguinal/femoral nodes. Approximately 50% of patients have fever, malaise, and anorexia. A smaller proportion experience weight loss and night sweats mimicking the presentation of lymphoma. Fever is usually low-grade but infrequently rises to $\geq 39^{\circ}\text{C}$. Resolution is slow, requiring

A PART 5 Infectious Diseases B C

D E F FIGURE 177-1 Manifestations of cat-scratch disease. A. Primary inoculation lesion. Axillary and epitrochlear lymphadenitis appeared 2 weeks later. B. Primary inoculation lesion. Submental lymphadenitis appeared 10 days later. C. Axillary lymphadenopathy of 2 weeks' duration. The overlying skin appears normal. D. Cervical lymphadenopathy of 6 weeks' duration. The overlying

skin is red. Thick, odorless pus (12 mL) was aspirated. E. Preauricular lymphadenopathy. F. Left-eye neuroretinitis. Note papilledema and stellate macular exudates (“macular star”).

weeks (for fever, pain, and accompanying signs and symptoms) to months (for node shrinkage). Atypical CSD occurs in 10–15% of patients in the absence or presence of lymphadenopathy. Atypical disease includes Parinaud’s oculoglandular syndrome (conjunctivitis with ipsilateral preauricular lymphadenitis; Fig. 177-1E), hepatosplenic disease, neuroretinitis (often presenting as unilateral deterioration of vision; Fig. 177-1F) and other ophthalmologic manifestations, neurologic manifestations (encephalitis, seizures, myelitis, facial and other cranial nerve palsies, peripheral neuritis), fever of unknown origin (FUO), pneumonitis, debilitating myalgia, arthritis or arthralgia (affecting mostly women

“ 20 years old), osteomyelitis (including multifocal disease), and dermatologic manifestations (including erythema nodosum [see Fig. A1-39], sometimes accompanying arthropathy). CSD-associated FUO is a unique syndrome that may be severe and debilitating, often mimics malignancy, and may present with multiorgan involvement, including hepatosplenic space-occupying lesions, abdominal/mediastinal lymph adenopathy, ocular disease, and multifocal osteomyelitis. Fever may be continuous or relapsing. Other manifestations and syndromes (e.g., idiopathic thrombocytopenic purpura, Henoch-Schönlein purpura, erythema multiforme [see Fig. A1-24A], myocarditis) also have been associated with CSD; however, a causal role for *B. henselae* has yet to be established. In elderly patients (>60 years old), lymphadenopathy is more often absent but encephalitis and FUO are more common than in younger patients. In immunocompetent individuals, CSD—whether typical or atypical—usually resolves without treatment and without sequelae, although some of the ophthalmologic manifestations may occasionally result in moderate to severe vision loss. Lifelong immunity is the rule. ■ ■DIAGNOSIS Routine laboratory tests usually yield normal or nonspecific results. Histopathology initially shows lymphoid hyperplasia and later demonstrates stellate granulomata with necrosis, coalescing microabscesses, and occasional multinucleated giant cells—findings that, although nonspecific, may narrow the differential diagnosis. Serologic testing (immunofluorescence or enzyme immunoassay) is the most commonly used laboratory diagnostic approach, with variable sensitivity and specificity. CSD serodiagnosis is often based on the presence of IgG alone (i.e., in the absence of IgM), and seroconversion may take a few weeks; these two factors may pose difficulties in the interpretation of serologic results. Other tests are of low sensitivity (culture, Warthin-Starry silver staining), of low specificity (cytology, histopathology), or of limited availability in routine diagnostic laboratories (polymerase chain reaction [PCR], immunohistochemistry). PCR of pus aspirated from lymph nodes or the primary inoculation lesion is highly sensitive and specific and is particularly useful for definitive and rapid diagnosis in seronegative patients. PCR of a lymph node biopsy specimen may be less sensitive, perhaps because of sampling error. APPROACH TO THE PATIENT Cat-

Scratch Disease A history of cat contact, a primary inoculation lesion, and regional lymphadenopathy—especially axillary/epitrochlear lymphadenopathy—are highly suggestive of CSD. A characteristic clinical course and corroborative laboratory tests make the diagnosis very likely. Conversely, when acute- and convalescent-phase sera are negative (as is the case in 10–20% of CSD patients), when spontaneous regression of lymph node size does not occur, and particularly when constitutional symptoms persist, malignancy must be ruled out. Pyogenic lymphadenitis, mycobacterial infection, brucellosis, syphilis, tularemia, plague, toxoplasmosis, sporotrichosis, and histoplasmosis also should be considered. In clinically suspected CSD in a seronegative individual, fine-needle aspiration may be adequate and PCR can confirm the diagnosis. When data are less supportive of CSD, lymph node biopsy rather than fine-needle aspiration is

preferred. In seronegative CSD patients with lymphadenopathy and severe complications (e.g., encephalitis or neuroretinitis), early biopsy is important to establish a specific diagnosis.

TREATMENT Cat-Scratch Disease (Table 177-2) Treatment regimens are based on only minimal data. Suppurative nodes should be drained by large-bore needle aspiration and not by incision and drainage to avoid chronic draining tracts. Systemic antibiotics are recommended in immunocompromised patients. **TABLE 177-2 Antimicrobial Therapy for Disease Caused by Bartonella Species in Adults** **DISEASE ANTIMICROBIAL THERAPY** Typical cat-scratch disease Not routinely indicated; for patients with extensive lymphadenopathy, consider azithromycin (500 mg PO

on day 1, then 250 mg PO once a day for 4 days) Cat-scratch disease neuroretinitis Value of systemic antibiotics is controversial, particularly when visual acuity is not significantly compromised. For more severe cases, doxycycline (100 mg PO bid) plus rifampin (300 mg PO bid) for 4–6 weeks is given. Consider adding systemic glucocorticoids. Other atypical cat-scratch disease manifestations As per neuroretinitis. Treatment duration should be individualized. **CHAPTER 177** Trench fever or chronic bacteremia with *B. quintana* Gentamicin (3 mg/kg IV once a day for 14 days) plus doxycycline (200 mg PO once a day or 100 mg PO bid for 6 weeks) Suspected Bartonella endocarditis Gentamicin^b (1 mg/kg IV q8h for ≥ 14 days) plus doxycycline (100 mg PO/IV bid for 6 weeks^c) plus ceftriaxone (2 g IV once a day for 6 weeks) Bartonella Infections, Including Cat-Scratch Disease Confirmed Bartonella endocarditis As for suspected Bartonella endocarditis minus ceftriaxone Bacillary angiomatosis Erythromycin^d (500 mg PO qid for 3 months) or Doxycycline (100 mg PO bid for 3 months) Bacillary peliosis Erythromycin^d (500 mg PO qid for 4 months) or Doxycycline (100 mg PO bid for 4 months) Carrión's disease Oroya fever Chloramphenicol (500 mg PO/IV qid for 14 days) plus another antibiotic (β -lactam preferred) or Ciprofloxacin (500 mg PO bid for 10 days) $\pm$ ceftriaxone (1–2 g IV once a day for 10 days) Verruga peruana Azithromycin (500 mg PO once a day for 7 days) or Ciprofloxacin (500 mg PO bid for 7–10 days) or Rifampin (10 mg/kg PO once a day, to a maximum of

600 mg, for 14 days) or Streptomycin (15–20 mg/kg IM once a day for 10 days) ^aData on treatment efficacy for encephalitis and hepatosplenic cat-scratch disease are lacking. Therapy similar to that given for neuroretinitis is reasonable. ^bSome experts recommend gentamicin at 3 mg/kg IV once a

day. If gentamicin is contraindicated, rifampin (300 mg PO bid) can be added to doxycycline for documented Bartonella endocarditis. cSome experts recommend extending oral doxycycline therapy for 3–6 months and measuring anti-Bartonella IgG titers every 8–10 weeks as a guide to duration of therapy, particularly when the infected valve was not resected. dOther macrolides are probably effective and may be substituted for erythromycin or doxycycline. Source: Recommendations are modified from JM Rolain et al: Antimicrob Agents Chemother 48:1921, 2004.

■ ■PREVENTION Avoiding cats (especially kittens) and instituting flea control are options for immunocompromised patients and for patients with valvular heart disease.

TRENCH FEVER AND CHRONIC BACTEREMIA ■ ■DEFINITION AND ETIOLOGY Trench fever, also known as 5-day fever or quintan fever, is a febrile illness caused by *B. quintana*. It was first described as an epidemic in the trenches of World War I; however, recent paleomicrobiological studies have provided evidence that *B. quintana* has been associated with human infection for 4000 years. This infection recently reemerged as chronic bacteremia seen most often in homeless people, also referred to as urban or contemporary trench fever. ■ ■EPIDEMIOLOGY In addition to epidemics in World Wars I and II, sporadic outbreaks of trench fever have been reported in many regions of the world. The human body louse has been identified as the vector and humans as the only known reservoir for human infections. Recently, macaque monkeys from China and Japan also were found to be natural hosts of *B. quintana*, without evidence for macaque-to-human transmission. After a hiatus of several decades during which trench fever was almost forgotten, small clusters of cases of *B. quintana* chronic bacteremia were reported sporadically, primarily from the United States and France, in homeless people without HIV infection. Alcoholism and louse infestation were identified as risk factors. PART 5 Infectious Diseases ■ ■CLINICAL MANIFESTATIONS The typical incubation period is 15–25 days (range, 3–38 days). “Classic” trench fever, as described in 1919, ranges from a mild febrile illness to a recurrent or protracted and debilitating disease. Fever is often periodic, lasting 4–5 days with 5-day (range, 3- to 8-day) intervals between episodes. Other symptoms and signs include headache, back and limb pain, profuse sweating, shivering, myalgia, arthralgia, splenomegaly, a maculopapular rash in occasional cases, and nuchal rigidity in some cases. Untreated, the disease usually lasts 4–6 weeks. Death is rare. The clinical spectrum of *B. quintana* bacteremia in homeless people ranges from asymptomatic infection to a febrile illness with headache, severe leg pain, and thrombocytopenia. Endocarditis sometimes develops. ■ ■DIAGNOSIS Definitive diagnosis requires isolation of *B. quintana* by blood culture. Some patients have positive blood cultures for several weeks. Patients with acute trench fever typically develop significant titers of antibody to Bartonella, whereas those with chronic *B. quintana* bacteremia may be seronegative. Patients with high titers of IgG antibodies should be evaluated for endocarditis. In epidemics, trench fever should be differentiated from epidemic louse-borne typhus and relapsing fever, which occur under similar conditions and share many features. TREATMENT *B. quintana* Bacteremia (Table 177-2) In a small, randomized, placebo-controlled trial involving homeless people with *B. quintana* bacteremia, therapy with gentamicin and doxycycline was superior to administration of placebo in eradicating bacteremia. Treatment of bacteremia is important, even in clinically mild cases, to prevent endocarditis. Optimal therapy for trench fever without documented bacteremia is uncertain.

BARTONELLA ENDOCARDITIS ■ ■DEFINITION AND ETIOLOGY *Coxiella burnetii* (Chap. 192) and Bartonella species are the most common pathogens of culture-negative endocarditis (Chap. 133). In

France, for example, *Bartonella* species were identified as the etiologic agents in 28% of 348 cases of culture-negative endocarditis. Prevalence, however, varies by geographic location and epidemiologic setting. *B. quintana* and *B. henselae* are the most common *Bartonella* species implicated in endocarditis, and other *Bartonella* species have reportedly caused rare cases (Table 177-1).

■ ■ **EPIDEMIOLOGY** *Bartonella* endocarditis has been reported worldwide. Most patients are adults; more are male than female. Risk factors associated with *B. quintana* endocarditis include homelessness, alcoholism, and body louse infestation; however, individuals with no risk factors have had *Bartonella* endocarditis diagnosed as well. *B. henselae* endocarditis is associated with exposure to cats. Most cases involve native rather than prosthetic valves; the aortic valve accounts for ~60% of cases. Patients with *B. henselae* endocarditis usually have preexisting valvulopathy, whereas *B. quintana* often infects normal valves.

■ ■ **CLINICAL MANIFESTATIONS** Clinical manifestations are usually characteristic of subacute endocarditis of any etiology. However, a substantial number of patients have a prolonged, minimally febrile or even afebrile indolent illness, with mild nonspecific symptoms lasting weeks or months before the diagnosis is made. Initial echocardiography may not show vegetations. Acute, aggressive disease is rare.

■ ■ **DIAGNOSIS** Blood cultures, even with use of special techniques (lysis centrifugation or EDTA-containing tubes), are positive in only ~25% of cases—mostly those caused by *B. quintana* and only rarely those caused by *B. henselae*. Prolonged incubation of cultures (up to 6 weeks) is required. Serologic tests—either immunofluorescence or enzyme immunoassay—usually demonstrate high-titer ($\geq 1:800$) IgG antibodies to *Bartonella*. Because of cross-antigenicity, routine serology does not distinguish between *B. quintana* and *B. henselae* and may also be cross-reactive with other pathogens, such as *C. burnetii* and *Chlamydia* species. Approximately 40–50% of patients with Q fever endocarditis have antibodies that significantly react with *B. henselae* and/or *B. quintana*; however, in the majority of cases, IgG titers against the true pathogen are several dilutions higher than those for the pathogen causing the false-positive serology, thus allowing the correct diagnosis to be made. Identification of *Bartonella* to the species level is usually accomplished by application of PCR and DNA sequencing methods to valve tissue or, infrequently, blood specimens.

TREATMENT *Bartonella* Endocarditis (Table 177-2) For patients with culture-negative endocarditis suspected to be due to *Bartonella* species, empirical treatment consists of gentamicin, doxycycline, and ceftriaxone; the major role of ceftriaxone in this regimen is to adequately treat other potential causes of culture-negative endocarditis, including members of the HACEK group (Chap. 163). Once a diagnosis of *Bartonella* endocarditis has been established, ceftriaxone is discontinued. Aminoglycosides, the only antibiotics known to be bactericidal against *Bartonella*, should be included in the regimen for ≥ 2 weeks. Indications for valvular surgery are the same as in subacute endocarditis due to other pathogens; however, the proportion of patients who undergo surgery (~60%) is high, probably as a consequence of delayed diagnosis.

BACILLARY ANGIOMATOSIS AND PELIOSIS ■ ■ **DEFINITION AND ETIOLOGY** Bacillary angiomatosis (sometimes called bacillary epithelioid angiomas or epithelioid angiomatosis) is a disease of severely immunocompromised patients, is caused by *B. henselae* or *B. quintana*, and is characterized by neovascular proliferative lesions involving various organs. Both species cause cutaneous lesions; hepatosplenic lesions

are caused only by *B. henselae*, whereas subcutaneous and lytic bone lesions are more frequently associated with *B. quintana*. *Bartonella* angiogenic factor A, a proangiogenic autotransporter identified in *B. henselae*, activates the host vascular endothelial growth factor pathway to drive angiogenesis. Bacillary peliosis is a closely related angioproliferative disorder caused by *B.*

henselae and involving primarily the liver (peliosis hepatis) but also the spleen and lymph nodes. Bacillary peliosis is characterized by blood-filled cystic structures whose size ranges from microscopic to several millimeters. ■ ■ **EPIDEMIOLOGY** Bacillary angiomatosis and bacillary peliosis occur primarily in HIV-infected persons (Chap. 208) with CD4+ T-cell counts of <100/μL but also affect other immunosuppressed patients and, in rare instances, immunocompetent patients. The incidence has decreased since the introduction of effective antiretroviral therapy and the routine use of rifabutin and macrolides to prevent Mycobacterium avium complex infection in AIDS patients. Contact with cats or cat fleas increases the risk of B. henselae infection. Risk factors for B. quintana infection are low income, homelessness, and body louse infestation. ■ ■ **CLINICAL MANIFESTATIONS** Bacillary angiomatosis presents most commonly as one or more cutaneous lesions that are not painful and may be tan, red, or purple in color. Subcutaneous, often tender nodules, superficial ulcerated plaques (Fig. 177-2), and verrucous growths are also seen. Nodular forms resemble those seen in fungal or mycobacterial infections. Painful osseous lesions, most often involving long bones, may underlie cutaneous lesions and occasionally develop in their absence. Other organs are rarely involved. Patients usually have constitutional symptoms, including fever, chills, malaise, headache, anorexia, weight loss, and night sweats. In patients with advanced immunodeficiency, B. henselae and B. quintana are important causes of FUO. In osseous disease, lytic

FIGURE 177-2 Lesions of cutaneous bacillary angiomatosis (BA) in three severely immunocompromised AIDS patients. Left panel shows a 1.5-cm ulcerated, bleeding BA lesion with an erythematous base; middle panel shows numerous small, 2-mm, scattered angiomatous BA lesions; right panel shows a 2.0-cm friable BA lesion on the thigh. (Photos courtesy of Timothy Berger, MD; Jordan Tappero, MD, MPH; and Jane Koehler, MA, MD.)

lesions are generally seen on radiography, and technetium scan shows focal uptake. The differential diagnosis of cutaneous bacillary angiomatosis includes Kaposi's sarcoma, pyogenic granuloma, subcutaneous tumors, and verruga peruana. In bacillary peliosis, hypodense hepatic areas are usually evident on imaging.

■ ■ **PATHOLOGY** Bacillary angiomatosis consists of lobular proliferations of small blood vessels lined by enlarged endothelial cells interspersed with mixed infiltrates of neutrophils and lymphocytes, with predominance of the former. Histologic examination of organs with bacillary peliosis reveals small blood-filled cystic lesions partially lined by endothelial cells that can be several millimeters in size. Peliotic lesions are surrounded by fibromyxoid stroma containing inflammatory cells, dilated capillaries, and clumps of granular material. Warthin-Starry silver staining of bacillary angiomatosis and peliosis lesions reveals clusters of bacilli. Cultures are usually negative. ■ ■ **DIAGNOSIS** Bacillary angiomatosis and bacillary peliosis are diagnosed by histologic examination. Blood cultures may be positive. **TREATMENT** Bacillary Angiomatosis and Peliosis (Table 177-2) Prolonged therapy with a macrolide or doxycycline is recommended for both bacillary angiomatosis and bacillary peliosis. **CHAPTER 177** ■ ■ **PREVENTION** Reasonable strategies for HIV-infected persons consist of control of cat-flea infestation and avoidance of cat scratches (for prevention of Bartonella Infections, Including Cat-Scratch Disease