Survey of the Seroprevalence of *Bartonella quintana* in Homeless People

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Trench fever is caused by *Bartonella (Rochalimaea) quintana*, a small gram-negative rod that is transmitted by body lice. Recently, *B. quintana* infections in homeless patients have been reported in the United States and Europe. From October 1993 to October 1994, the seroprevalence of antibodies to *B. quintana* was assessed by indirect immunofluorescence in a prospective study of 221 nonhospitalized homeless people, 43 hospitalized homeless patients (cases), 250 blood donors, and 57 hospitalized matched controls. Four (1.8%) of 221 nonhospitalized homeless people tested had titers of >1:100. Of the 43 cases, seven (16%) had serological titers of ≥1:100. None of the 250 serum samples from blood donors contained antibodies to *B. quintana*. The presence of antibodies to *B. quintana* in cases was significantly associated with the presence of body lice, exposure to cats, headaches, eastern European origin, and pain in the legs. This study demonstrates the presence of antibodies to *B. quintana* in the homeless population and should alert physicians that *B. quintana* might be an etiologic agent of fever in homeless patients.

Trench fever is an infection due to *Bartonella* (formerly *Rochalimaea*) *quintana* [1] that was described in early 1915 during World War I by Graham, Rankin, and Hunt [2, 3]. Soon after the first reported case of trench fever [4], investigators emphasized that the disease usually occurred in persons in frequent contact with one another [5]. In 1917, Pappenheimer and Mueller succeeded in transmitting the disease to one of three volunteers by allowing lice to feed first on several patients with trench fever and then on the volunteers [6]. Cold weather was also a chief epidemiologic factor since it led to the wearing of underclothing for long periods and kept people indoors and in close contact [2].

Trench fever has long been regarded mainly as an old disease that prevailed only during wartime; however, recent reports [7, 8] have stressed that the disease may be returning in industrialized countries. Recently, new cases of *B. quintana* infection have been reported in the United States and France [9–12]. *B. quintana* bacteremia in homeless people in Seattle has been documented [13]. Cases of apparent "culture-negative" endocarditis due to *B. quintana* have also been described in homeless patients [14, 15] and in an HIV-positive patient [16], and a typical case of trench fever has recently been reported [17]. Because the number of homeless people in industrialized countries is increasing dramatically and because of associated louse outbreaks, we evaluated the prevalence of *B. quintana* infection in homeless people.

Patients and Methods

To investigate the seroprevalence of antibodies to *B. quintana* in hospitalized homeless patients (cases), a prospective study was carried out in an infectious diseases unit from October 1993 to October 1994. All cases were hospitalized following presentations to the emergency department. Patients were said to be homeless if they had no personal home address (not including shelters or other addresses of well-known services for homeless individuals) and lived in the street. At the time of presentation, all cases underwent a complete physical examination, and epidemiologic and clinical data were recorded. WBC and RBC counts and levels of liver enzymes and lactate dehydrogenase were determined, and blood cultures and serological testing for *B. quintana* were performed. Six milliliters of heparinized blood from each case was inoculated onto blood agar and incubated at 32°C for 6 weeks for isolation of *Bartonella*. Roentgenograms of the lungs of all cases were obtained. Depending on the findings of the films, other investigations were carried out.

Controls were chosen from patients hospitalized in the same unit during the same study period; these controls were matched with the cases according to sex, age, time of the year, and the clinical presentation at the time of admission.

To evaluate the seroprevalence of antibodies to *B. quintana* in nonhospitalized homeless individuals, one of the authors (P.H.) visited shelters and obtained blood samples from 221 homeless people. A drop (20 μL) of blood from each person was placed onto blotting paper, and an anonymous number was assigned to each drop of blood. The age, sex, area of living, time of residence in France, and country of origin of

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Table 1. Serum antibody titers of *Bartonella quintana*–positive homeless patients who were hospitalized.

Patient no.	*B. quintana* Serum sample 1 IgG†	*B. quintana* Serum sample 1 IgM‡	*B. quintana* Serum sample 2 IgG	*B. quintana* Serum sample 2 IgM	*Bartonella henselae** IgG	*Bartonella henselae** IgM
1	800	0	800	0	200	0
2	100	0	ND	ND	0	0
3	200	0	ND	ND	0	0
4	100	0	ND	ND	0	0
5	800	0	400	0	0	0
6	400	25	800	25	0	0
7	50	0	200	0	0	0

NOTE. ND = not determined.
* Only one serum sample.
† Titers were significant if ⩾1:100.
‡ Titers were significant if ⩾1:25.

each person was also recorded. The blotting papers were then washed in 500 μL of PBS overnight at room temperature. The supernatant (1:25 dilution) was then diluted to 1:50 and 1:100 in PBS before being processed by indirect immunofluorescence.

Blood specimens from cases and controls were prepared in the same way. Serum from a patient with a titer of 1:800 was used as a positive control. A negative blood sample was obtained from a seronegative blood donor. The seroprevalence of antibodies to *B. quintana* in the general population was established with 250 serum samples from blood donors.

Serology was performed at the National Center for Rickettsioses in Marseille, France. The antigen used was *B. quintana* "Oklahoma," a strain isolated from an HIV-infected man [18]; it was kindly provided by G. A. Dasch (Naval Medical Research Institute, Bethesda, MD). The antigen was grown on the human endothelial cell line ECV 304.9 (Cerdic, Valbonne, France) and was preserved in 0.1% sodium azide. A fluorescein isothiocyanate–labeled goat antibody to human IgG and IgM was used to reveal the presence of antibody to *B. quintana*. The cutoff titers were determined from serological data for the blood donors as ⩾1:100 for IgG and ⩾1:25 for IgM. All serum samples were also tested in a similar manner for the presence of antibodies to *Bartonella henselae* with use of *B. henselae* Houston 1 (ATCC 49793) as the antigen.

All data for cases and controls were computerized, and the statistical analysis was performed by means of Epi-Info Version 5.01 software (Centers for Disease Control and Prevention, Atlanta). Frequencies were compared with use of Fisher's exact test, and the Student's *t*-test was used to compare means. Differences were considered significant when the *P* value was $<.05$.

Results

Between October 1993 and October 1994, 43 homeless patients were hospitalized. Of these cases, seven (16%) had titers of IgG to *B. quintana* of ⩾1:100 (table 1). One of these seven cases had documented *B. quintana* endocarditis; this case has been previously reported [15]. One case also had antibodies to *B. henselae*. None of the 57 controls had positive serology. When cases were compared with controls, the cases had significantly more sweat ($P = .03$), dizziness ($P = .006$), tibial pain ($P = .0004$), pruritus ($P = .005$), headaches ($P = .03$), and hepatomegaly ($P = .02$). They also had significantly more body lice ($P = .005$) and drank more alcohol ($P = .0002$).

To evaluate if *B. quintana*–seropositive cases had clinical and epidemiologic signs of trench fever, we compared the symptoms of the 36 seronegative cases with those of the seven seropositive cases. The seropositive group had significantly more headaches ($P = .01$) and splenomegaly ($P = .02$) than did the seronegative group; seropositive cases also had significantly more contact with cats ($P = .02$) (table 2).

A serological study of the 221 nonhospitalized homeless people was carried out. The seroprevalence of antibodies to *B. quintana* in this group was 1.8% (four of 221). Three people had IgG titers of 1:100, and one person had an IgG titer of 1:3,200. None of the 250 blood donors tested had titer of ⩾1:100. The difference in seroprevalence between the two groups was significant ($P = .0477725$).

Discussion

Trench fever has been known as 5-day fever, quintan fever, and Wolhynia fever [19]. Trench fever is a blood infection due to *B. quintana* that is transmitted by the human body louse *Pediculus humanus* [6]. *B. quintana* is conveyed by the excreta of infected lice, which may enter the body through broken skin or intact conjunctiva [2]. Thus, poor socioeconomic conditions enhance the transmission of *B. quintana* [20]. Because the number of homeless people in industrialized countries is increasing dramatically and because of associated louse outbreaks, it is not surprising to find such a high number of hospitalized homeless patients who have been in contact with *B. quintana*. Moreover, since the fall of the Berlin Wall, more and more young people from eastern European countries travel in western Europe.

Surprisingly, the seroprevalence of antibodies to *B. quintana* in nonhospitalized homeless people was significantly ($P = .008$) lower than that in cases (hospitalized homeless patients) (1.8% vs. 16%, respectively). This occurrence might be explained by the fact that the cases were significantly older than the nonhospitalized homeless people (48.8 ± 9.7 years vs. 35.7 ± 12.5 years, respectively) and thus may have been exposed to risk factors longer than the nonhospitalized homeless people. Moreover, these results also could be biased by the fact that the people at the shelters from whom blood samples were drawn may not be representative of the general homeless population and may be particularly healthy compared with the cases.

Table 2. Epidemiologic, clinical, and laboratory findings associated with the presence of antibodies to *Bartonella quintana* in hospitalized homeless patients.

Finding or characteristic	No. (%) of patients		*P* value
	B. quintana–seronegative patients* (n = 36)	*B. quintana*–seropositive patients† (n = 7)	
Male sex	34 (94.4)	7 (100)	NS
Alcohol use	33 (91.7)	6 (85.7)	NS
Tobacco use	30 (83.3)	5 (71.4)	NS
Toxic	4 (11.1)	2 (28.6)	NS
Dog exposure	2 (5.6)	2 (28.6)	NS
Cat exposure	0	2 (28.6)	.02‡
Cattle exposure	0	0	NS
Rodent exposure	0	0	NS
Tick exposure	1 (2.8)	1 (14.3)	NS
Lice exposure	4 (11.1)	2 (28.6)	NS
Fever	12 (33.3)	2 (28.6)	NS
Asthenia	22 (61.1)	4 (57.1)	NS
Weight loss	18 (50)	4 (57.1)	NS
Anorexia	16 (44.4)	4 (57.1)	NS
Sweat	4 (11.1)	0	NS
Dizziness	1 (2.8)	1 (14.3)	NS
Depression	4 (11.1)	0	NS
Leg pain	19 (52.8)	3 (42.9)	NS
Pruritus	9 (25)	3 (42.9)	NS
Rash	4 (11.1)	1 (14.3)	NS
Headaches	4 (11.1)	4 (57.1)	.01‡
Pollakiuria	4 (11.1)	2 (28.6)	NS
Precordialgia	2 (5.6)	0	NS
Dyspnea	10 (27.8)	4 (57.1)	NS
Palpitations	0	0	NS
Conjunctivitis	1 (2.8)	0	NS
Hepatomegaly	13 (36.1)	5 (71.4)	NS
Splenomegaly	0	1 (14.3)	.02‡
Cardiac murmur	2 (5.6)	1 (14.3)	NS
Anemia	25 (69.4)	6 (85.7)	NS
Elevated WBC count	7 (19.4)	3 (42.9)	NS
Elevated hepatic enzyme levels	12 (33.3)	4 (57.1)	NS

NOTE. NS = not significant.
* Mean age ± SD = 48.8 ± 13.3 years (NS).
† Mean age ± SD = 48.1 ± 9.7 years (NS).
‡ Significant finding.

Despite the fact that the body louse has been implicated as the vector of trench fever [21], contact with cats was strongly associated with the presence of antibodies to *B. quintana* in our study. Because of an antigenic cross-reaction between *B. henselae* and *B. quintana*, one may suggest that our cases were exposed to *B. henselae*–infected cats. In fact, only one case had antibodies to *B. henselae,* and he denied having contact with cats.

The incubation period of trench fever may vary from 15 to 25 days. A wide range of clinical manifestations of trench fever have been reported, ranging from asymptomatic infections to severe diseases [6]. The onset of the disease is usually sudden with a prodromal period lasting for ⩾2 days.

Clinical symptoms appear in the following order: headaches, weakness, pain in the legs, malaise, dyspnea, dizziness, pain in the loins, shivering, pain in the abdomen, diarrhea, constipation, anorexia, nausea, frequent micturition, restlessness, and insomnia [22]. The headaches are most often severe, and the pain in the legs is typically felt in the bones, most frequently the tibiae [3]. Physical examination often reveals an enlarged spleen, although hepatomegaly is infrequent. Fever is variable, often occurring periodically or irregularly. In fact, an acute onset of a periodic febrile illness with headaches and pain in the shins is characteristic [23].

In our study, cases more frequently abused alcohol, which may explain the increased frequency of dizziness, leg pain (polyneuritis), headaches, and hepatomegaly in cases compared with controls. However, except for headaches, these symptoms were not significantly associated with the presence of antibodies to *B. quintana.* This finding correlates with the results of indirect immunofluorescence, as only one case had signifi-

cant titers of IgM (which indicate an acute illness). This case's diagnosis was *B. quintana* endocarditis, a newly recognized clinical entity [14, 15].

Thus, none of the cases in this study, except for the case with endocarditis, had acute infection; therefore, it is likely that the antibodies to *B. quintana* that were detected were serological hallmarks of past infections. Splenomegaly was only observed in the seropositive case with endocarditis. Consequently, this symptom cannot be considered characteristic of trench fever.

In conclusion, a significant titer of antibodies to *B. quintana* was found in 16% of cases (hospitalized homeless patients). The high seroprevalence of antibodies to *B. quintana* in the homeless population should alert physicians that an acute onset of a periodic febrile illness with headaches and pain in the shins in a homeless person exposed to lice, cats, or dogs might be caused by *B. quintana*.

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