

homeless people, 16% had high antibody titers to *B. quintana*. Subsequently, Brouqui and colleagues (3) investigated *B. quintana* infections among all homeless people who presented to the emergency departments of hospitals in Marseille, France during 1997. A total of 71 people were included in the study, with 10 (14%) yielding *B. quintana* on blood culture and 21 (30%) possessing serological evidence of infection. Most recently, Smith and colleagues (25) reported a seroprevalence of 10% among 200 mainly homeless attendees of a free clinic in Los Angeles. Two other surveys have targeted inner city intravenous drug users, many of whom were homeless. In the earlier of these, 10% of 630 residents of Baltimore screened had serological evidence of *B. quintana* exposure (6), whereas in the latter study (7), involving 204 New York drug users, a seroprevalence of only 2% was recorded (although almost half had antibodies against other *Bartonella* spp.). From these data, our findings are not at all out of keeping with what has been observed previously elsewhere in the world.

Contemporary urban trench fever was first reported less than 10 years ago, and thus medical and scientific analysis of the syndrome remains nascent (26). In developed countries, trench fever is predominantly encountered among the urban poor or the homeless. The susceptibility of these individuals is likely to result from their reduced immune status and frequent contact with body lice infected with *B. quintana*. As none of the homeless people included in our survey had been hospitalized during the preceding several months, we were not able to ascertain whether they had any immune suppressive infections (e.g., human immunodeficiency virus), but we were able to confirm that a significant proportion of our sample were exposed to body lice. Our estimate of prevalence of body lice infestation (11%) is similar to the figure of 7% obtained in an earlier sampling of a similar population in Tokyo (24). The Japanese homeless community has been growing since the economic downturn in the 1990s, and with no concerted intervention strategies for louse infestation being adopted, we predict that an increasing number of people will be exposed to body lice and the pathogens they transmit. To further emphasise that prolonged homelessness will also inevitably lead to pathogen exposure, we, like others, found a positive association between the length of time spent homeless and the risk of infection by *B. quintana*.

Confounding a wider recognition of trench fever by the medical community is not solely the nature of the most susceptible population. *B. quintana* infections are insidious, most often devoid of acute symptoms but inducing manifestations as a result of extreme chronicity. Brouqui and colleagues (2) reported that even an outbreak of trench fever cannot be readily clinically diagnosed, finding that among infected individuals, all symptoms except for a headache were not significantly associated with the presence of antibodies to *B. quintana*.

Laboratory diagnosis of *B. quintana* infections is also very problematic. As we observed, a broad-based adoption of recommended cut-off titers, even for commercially-available kits, is impractical, and, as previously suggested, researchers would be wiser to evaluate the study population and adjust cut-off titers accordingly (19). Unfortunately, we could not determine the cut-off titer for diagnosing trench fever, although the cut-off titer of ≥ 256 in IgG antibodies seems to be adequate to evaluate the seroprevalence of *B. quintana* in our surveillance. In previous serological studies, the specificity of assays has varied, typically between 70 and 99% (10,11,22,32), such that cut-off titers for bartonella diagnosis were

encountered among 9% of healthy Greeks (28) and 16% of healthy Germans (22). One explanation for the apparent high seropositive rates in these and our healthy populations may be the lack of specificity of assays due to cross-reaction with other common pathogens. Cross-reaction between *Bartonella* spp. is well recognized (31), and cross reactivity between antigens of *Bartonella* and antigens derived from *Coxiella burnetii*, *Anaplasma phagocytophilum* and *Chlamydia* spp. has also been reported (8,13,17). Molecular diagnostic techniques should provide more clear-cut evidence of infections. However, evaluating the sensitivity of this approach is difficult given the unreliability of other diagnostic criteria. As others have done, we found no significant correlation between PCR results and serological titers, because the IgG response usually occurred 1-2 weeks after the infection of viral or bacterial infection. There is also a possibility that the detection of the *Bartonella* gene is derived from traces of previous infection. Our failure to isolate *B. quintana* from PCR-positive (or any other) individuals was disappointing, given that we adopted a protocol that has been used successfully elsewhere in the world (14). Why we failed is unclear, although it is interesting to note that isolation rates in some parts of the world (e.g., Australia) (10) are significantly higher than elsewhere. Geographic variation in reagent composition may occur, or there may be variation in the intrinsic "culturability" of the bartonellae themselves. From another point of view, targeted homeless people are non-hospitalized and almost none of the people showed typical symptoms of trench fever in our outreach program. Therefore, there is practically no possibility of encountering patients with bacteremia or trench fever in our surveillance.

Only very few physicians understand the current status of trench fever. However, the high IgG antibody titers to *B. quintana* and the presence of *B. quintana* DNA in the blood of the Japanese homeless population suggest that trench fever should be considered in the differential diagnosis of patients in emergency hospitals and even in small clinics, and a specific medical examination should be performed. Moreover, medical staff, sanitary inspectors, health workers and social workers working in health and welfare sections of municipal governments should be aware of the possibility of bartonellosis in the populations they attend to or care for. Further efforts to diagnose and control trench fever should be intensified in local public health offices of the larger cities in Japan.

ACKNOWLEDGMENTS

We would like to thank the people of P city for their permission to carry out the study and their cooperation throughout, and the authorities and staff of the P city municipal agency for facilitating our body lice research.

The ethical committees of the P city government and National Institute of Infectious Diseases granted ethical clearance.

This study was supported in part by the Research Grants of the Research on Emerging and Re-emerging Infectious Diseases from the Japanese Ministry of Health, Labour and Welfare.

We are also indebted to Drs Michael Chance and Ian Hasting of the Liverpool School of Tropical Medicine for their help with statistical analysis, and to Dr Richard Birtles for his careful review of the manuscript and useful suggestions.

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