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## Brill-Zinsser Disease in Moroccan Man, France, 2011

**To the Editor:** Epidemic typhus is caused by *Rickettsia prowazekii* and transmitted by human body lice. For centuries, it has been associated with overcrowding, cold weather, and poor hygiene. Brill-Zinsser disease is a recurrent form of epidemic typhus that is unrelated to louse infestation and develops sporadically years after the primary illness. Clinical features are similar to, but milder than, those of epidemic typhus (1). We report a case of Brill-Zinsser disease in a patient who was born in Morocco and had no history of epidemic typhus.

A 69-year-old man living in France sought care from his general practitioner on March 7, 2011, after 2 days of high-grade fever (40°C) associated with headache, myalgia, fatigue, and mild cough. Amoxicillin was prescribed for a putative diagnosis of acute respiratory infection.

He was admitted to hospital on March 9 for persistent fever. Physical examination results were unremarkable. Blood test results were as follows: C-reactive protein 111 mg/L (reference 0–8 mg/L); procalcitonin 0.49 ng/mL (reference 0.1–0.4 ng/mL), lymphocyte count  $0.7 \times 10^3$  cells/ $\mu$ L (reference  $1\text{--}4 \times 10^3$  cells/ $\mu$ L), platelet count  $92 \times 10^3$  cells/ $\mu$ L (reference  $150\text{--}450 \times 10^3$  cells/ $\mu$ L), and lactate dehydrogenase 376 U/L (reference 94–246 U/L). Chest radiograph results were normal. Results of 5 blood cultures and a urine culture were negative. Stupor developed on March 11. Cerebrospinal fluid test results were normal. Because the patient lived near a goat farm, Q fever and tularemia were considered plausible hypotheses, and oral doxycycline was introduced on March 13. The patient became afebrile on March 15, and he was discharged from the hospital and

remained well.

On the basis of serologic results, the following diagnoses could be ruled out: viral infections (HIV, cytomegalovirus, Epstein-Barr virus); tularemia; Q fever; leptospirosis; salmonellosis; and *Legionella*, *Mycoplasma*, and *Chlamydia* spp. infections. Acute-phase and convalescent-phase serum samples were positive for typhus-group rickettsiae by the microimmunofluorescence assay at the World Health Organization Collaborative Center for Rickettsioses and Other Arthropod-Borne Bacterial Diseases (Marseille, France). A microimmunofluorescence assay showed titers of 100 for IgM and 6,400 for IgG. Western blot analyses and cross-adsorption studies strongly suggested *R. prowazekii* as the cause of the man's illness. Quantitative PCR result on DNA extracted from the acute-phase serum was negative (2).

The patient had been raised in Morocco. At 19 years of age, he emigrated to France, where he lived in a urban area. He subsequently traveled every 3 years to Morocco for 1-month summer holidays, always in urban areas. He had most recently traveled to Morocco in 2008. He denied any history of hospitalization for a severe febrile illness and any exposure to louse bites. In the weeks before disease onset, he had not taken any new drug. He had no immunoglobulin deficiency.

On the basis of serologic analysis with Western blot, we confirmed *R. prowazekii* infection in a patient with no recent travel and no contact with lice or flying squirrels. *R. prowazekii* infection may occur rarely in France; it was found in Marseille in 2002 in an asymptomatic homeless person (3). In contrast, the patient in our report was living in a hygienic environment, and an autochthonous infection is therefore highly unlikely.

Epidemic typhus was endemic to North Africa until the 1970s (4).

Subsequently, this region was thought to be free from epidemic typhus, but 2 cases have been reported since 1999 in Algeria, where 1 case of Brill-Zinsser disease was observed in a man who had had epidemic typhus in 1960 during the Algerian civil war (5–7). Few published data exist about the seroprevalence of *R. prowazekii* infections in North Africa (4). In Tunisia, no epidemic typhus was found in 2005 among 47 febrile patients (8). However, a seroepidemiologic survey performed in blood donors and hospitalized patients in the Aures, Algeria, found a prevalence of 2% (4). This finding suggests that *R. prowazekii* infection might have occurred in this population more often than suspected. No recent published data are available from Morocco.

Since 1970, reports of only 8 cases of Brill-Zinsser disease have been published (9,10). In all cases, known risk factors were present (overcrowding, poor hygiene, or contact with flying squirrels). Brill and Zinsser described that stress or waning immunity could reactivate *R. prowazekii* infection (2). Corticosteroids can trigger recurrence of *R. prowazekii* in mice (2), but no such observations were made in humans. In the case presented here, we found no stress factor, no immunosuppression, and no medical history of epidemic typhus.

Brill-Zinsser disease can develop >40 years after acute infection. The mechanism of *R. prowazekii* latency has not been established. A recently explored reservoir for silent forms of *R. prowazekii* infection is adipose tissue because it contains endothelial cells, which are the target cells for *R. prowazekii* infection, and because of its wide distribution throughout the body (2). Brill-Zinsser disease should be considered as a possible diagnosis for acute fever in any patient who has lived in an area where epidemic typhus is endemic.

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## Temperate Climate Niche for *Cryptococcus gattii* in Northern Europe

**To the Editor:** *Cryptococcus gattii* was considered to be geographically restricted to countries with tropical and subtropical climates until 1999, when an outbreak of cryptococcosis in humans and animals occurred in the temperate climate of Vancouver Island, British Columbia, Canada (1). Montagna et al. reported the first environmental *C. gattii* in Europe from the Mediterranean region of Italy; these authors isolated it from 11 (4.3%) of 255 samples of plant detritus of *Eucalyptus camaldulensis* trees collected from the residential locality of an autochthonous case of cryptococcal meningitis caused by *C. gattii* in Apulia (2). These observations were recently substantiated by the isolation of *C. gattii* from plant debris of trees belonging to *Ceratonia siliqua* (carob), *Pinus halepensis* (stone pine), and *E. camaldulensis* in Spain (3). We report environmental isolation of the primary pathogenic fungus *C. gattii* from a forest in Berg en Dal, the Netherlands, which extends its geographic distribution to the temperate climate of northern Europe.

We investigated 112 decayed wood samples collected from inside trunk hollows of 52 living trees belonging to 5 families during April–May 2011 in Nijmegen, the Netherlands. The trees sampled were chestnut (*Castanea sativa*, n = 24), Douglas fir (*Pseudotsuga menziesii*, n = 17), oak (*Quercus macranthera*, n = 6), walnut (*Juglans regia*, n = 3), and mulberry (*Morus alba*, n = 2). The main criterion in selecting a tree for sampling was advanced age and presence of large trunk hollows variably sheltered from sunlight. The sampled sites had no bird nests and were apparently free from avian excreta. The decayed wood samples were collected with an in-house swabbing technique by using simplified Staib niger seed agar as described (4). The plates were incubated at 30°C and periodically observed up to 7 days for isolation of *C. gattii* and *C. neoformans*. Suspected colonies of *Cryptococcus* spp. were purified by dilution plating and identified by their morphologic and biochemical profiles, including development of blue color on L-canavanine-glycine bromothymol blue medium.

Identity of the isolates was confirmed by sequencing the internal transcribed spacer and D1/D2 regions, and they were genotyped by using amplified fragment-length polymorphism (AFLP) fingerprinting and multilocus sequence typing (MLST). The MLST loci *CAP10*, *CAP59*, *GPD1*, *IGS*, *LAC1*, *MPD1*, *PLB1*, *SOD1*, *TEF1a*, and *URA5* of the environmental *C. gattii* isolates were amplified and sequenced, and data were compared with MLST data from a large *C. gattii* population study (5) and with a recently published set of clinical, animal, and environmental *C. gattii* isolates from Mediterranean Europe and the Netherlands (Figure) (3,6,7). In addition, the mating type was determined with PCR by using mating type-specific primers for the *STE12a* and  $\alpha$  alleles (8).