Borrelia mayonii: prying open Pandora's box of spirochetes

Bobbi Pritt and colleagues[1] reveal that *Borrelia mayonii* is a new member of the *Borrelia burgdorferi* sensu lato complex, and show that this spirochete is pathogenic to human beings. However, the authors err on several key points. They state *B burgdorferi* sensu stricto was previously the only cause of Lyme borreliosis in the USA. With the discovery of *B mayonii*, they take credit for describing the first non-*B burgdorferi* sensu stricto in patients in the USA; this assumption is not true. Girard and colleagues[2] reported *B bissettii* in patients in California and Clark and colleagues[3] documented *B americana* and *B andersonii* in human blood from residents in the southeastern USA. Furthermore, Rudenko and colleagues[4] reported a *B bissettii*-like strain in a Florida patient. In all of these cases, patients had clinical symptoms commonly associated with Lyme borreliosis.

In their Introduction, Pritt and colleagues state that *B garinii*, *B afzelii*, and *B burgdorferi* sensu stricto are the only *B burgdorferi* sensu lato genospecies that cause Lyme borreliosis in Europe. In fact, at least five genospecies of the *B burgdorferi* sensu lato complex are pathogenic to human beings, including *B afzelii*, *B bavariensis*, *B burgdorferi* sensu stricto, *B garinii*, and *B spielmanii*.[5] Additionally, *B bissettii*, *B kurtenbachii*, *B lusitaniae*, and *B valaisiana* have been reported in patients in Europe.[5–7] The authors state that *B burgdorferi* sensu lato has never been reported in peripheral blood, but actually several researchers in the USA and Europe have isolated spirochetes from blood.[4,5]

Biogeographically, the unique strain of *B burgdorferi* sensu lato (W97F51) from southeastern Wisconsin was completely overlooked.[8] This novel strain was reported before *B mayonii*, and should have been addressed in both the text and the phylogenetic analyses (figure 4 in the Article).

Furthermore, the authors contend that Wisconsin is the epicentre of *B mayonii*; however, migratory songbirds play a vital part in the epidemiology of Lyme disease vector ticks, including the blacklegged tick (*Ixodes scapularis*).[9] Since passerine migrants transport *I scapularis* immatures thousands of kilometres during bidirectional, spring and fall migration, these avian hosts will, undoubtedly, disperse *B mayonii* spirochetes much further than currently recognised.

The authors claim that *B mayonii* causes symptoms that distinguish it from other *B burgdorferi* sensu lato genospecies. With only six patients, however, it seems audacious to state that *B mayonii* clinical symptoms are distinct from patients infected with *B burgdorferi* sensu stricto. The authors laud the US Food and Drug Administration-approved Lyme disease test kits, but some patients were seronegative. Based on the recommended two-tiered algorithm (table 2 in the Article), patient 6 was entirely negative and the other patients had inconsistent serological results. Finally, the authors recommend standard, short-term treatment for *B mayonii*, but fail to mention the limitations of this treatment for persistent Lyme disease.[10]

I declare no competing interests.

John D Scott
jkscott@bserv.com

Lyme Ontario, Research Division, Fergus, ON, Canada

1 Pritt BS, Mead PS, Hoang Johnson DK, et al. Identification of a novel pathogenic *Borrelia* species causing Lyme borreliosis with unusually high spirochaetaemia: a descriptive study. *Lancet Infect Dis* 2016; **16:** 556–64.

2 Girard YA, Fedorova N, Lane RS. Genetic diversity of *Borrelia burgdorferi* and detection of *B bissettii*-like DNA in serum of north-coastal residents. *J Clin Microbiol* 2011; **49:** 945–54.

3 Clark KL, Leydet B, Hartman S. Lyme borreliosis in human patients in Florida and Georgia, USA. *Int J Med Sci* 2013; **10:** 915–31.

4 Rudenko N, Golovchenko M, Vancová M, Clark K, Grubhoffer L, Oliver JH Jr. Isolation of live *Borrelia burgdorferi* sensu lato spirochetes from patients with undefined disorders and symptoms not typical for Lyme borreliosis. *Clin Microbiol Infect* 2016; **22:** 267, e9–e15.

5 Golovchenko M, Vancová M, Clark K, Oliver JH Jr, Grubhoffer L, Rudenko N. A divergent spirochete strain isolated from a resident of the southeastern United States was identified by multilocus sequence typing as *Borrelia bissettii*. *Parasit Vectors* 2016; **9:** 68.

6 Rudenko N, Golovchenko M, Mokracek A, et al. Detection of *Borrelia bissettii* in cardiac valve tissue of a patient with endocarditis and aortic valve stenosis (Czech Republic). *J Clin Microbiol* 2008; **46:** 3530–43.

7 Collares-Pereira M, Couceiro S, Franca I, et al. First isolation of *Borrelia lusitaniae* from a human patient. *J Clin Microbiol* 2004; **42:** 1316–18.

8 Caporale DA, Johnson CM, Millard BJ. Presence of *Borrelia burgdorferi* (Spirochaetales: Spirochaetaceae) in southern Kettle Moraine State Forest, Wisconsin, and characterization of strain W97F51. *J Med Entomol* 2005; **42:** 457–72.

9 Scott JD, Anderson JF, Durden LA. Widespread dispersal of *Borrelia burgdorferi*-infected ticks collected from songbirds across Canada. *J Parasitol* 2012; **98:** 49–59.

10 Cameron DJ, Johnson LB, Maloney EL. Evidence assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. *Expert Rev Anti Infect Ther* 2014; **12:** 1103–35.

Authors' reply

We thank John Scott for his comments regarding our recent Article[1] describing the identification of a novel genospecies of *Borrelia burgdorferi* sensu lato (*Borrelia mayonii*) as a new cause of Lyme borreliosis among patients in the upper midwestern USA. We agree with Scott that multiple *B burgdorferi* sensu lato genospecies can infect human beings. Our wording "nearly all human infections are caused by three *B burgdorferi* sensu lato genospecies" reflects this, and does not exclude other *B burgdorferi* sensu lato genospecies. A more thorough review of *B burgdorferi* sensu lato genospecies was neither within the focus of our Article nor possible due to the word limit. We concur that studies on other *B burgdorferi* sensu lato genospecies as a cause of Lyme borreliosis in North America and Europe are important.

Scott suggests that we state that *B burgdorferi* sensu lato has never been reported from peripheral blood. To clarify, in the introduction we state "microscopic detection" of *B burgdorferi* sensu lato spirochaetes has never been reported in peripheral blood. This is an important distinction given that a major finding of our study is that *B mayonii* causes Lyme borreliosis with unusually high spirochaetaemia. Scott questions why *Borrelia* species W97F51 was not included in figure 4. We point out that *Borrelia* species W97F51 is included in the phylogenetic tree in figure 4A of the web appendix; this analysis shows that it is distinct from *B mayonii*. Scott suggests that the geographical distribution and clinical presentation of *B mayonii* has not been fully defined. We agree and believe we addressed this in the last paragraph of the Article, where we highlight the need to better define the clinical range of illness and establish the geographical distribution of infected human beings and ticks. With regard to the results of serological testing, we note that the negative results were discussed in our Article. We expand here by clarifying that a negative result is expected early after illness onset when using a diagnostic test that is dependent on detecting the host's production of antibodies. This is among the reasons why we suggested the addition of *oppA1* PCR for direct detection and diagnosis of *B mayonii*. Finally, we would like to note that treatment for persistent Lyme disease goes beyond the scope of our Article. We hope our findings encourage more studies on *B mayonii* as well as physician awareness of this new genospecies to ensure infected patients are diagnosed and treated promptly.

BSP is employed by Mayo Clinic, which provides commercial PCR and serologic laboratory testing for *Borrelia burgdorferi* and related species through its reference laboratory, Mayo Medical Laboratories. BSP received partial funding for this project from the Mayo Clinic Department of Laboratory Medicine and Pathology Small Grant Program. JMP declares no competing interests. The views and conclusions in this letter are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

*Bobbi S Pritt, Jeannine M Petersen
pritt.bobbi@mayo.edu

Mayo Clinic, Rochester, MN, USA (BSP); and Division of Vector Borne Diseases, US Centers for Disease Control and Prevention, Fort Collins, CO, USA (JMP)

1 Pritt BS, Mead PS, Hoang Johnson DK, et al. Identification of a novel pathogenic *Borrelia* species causing Lyme borreliosis with unusually high spirochaetaemia: a descriptive study. *Lancet Infect Dis* 2016; **16:** 556–64.

Steroid use and clinical sequelae in two survivors of EVD

John Mattia and colleagues[1] described the clinical sequelae during early Ebola viral disease (EVD) convalescence in a cohort of 277 survivors in Sierra Leone: arthralgias (76%), new ocular symptoms (60%), and uveitis (18%) were the more common presentations. Ebola viral load at the time of EVD diagnosis was the independent predictor of ocular symptoms, and specifically uveitis.

In Rome, Italy, we successfully treated two Italian patients with EVD who had a high viral load at the time of diagnosis (5×10^6 copies per µL and 5×10^7 copies per µL, respectively). Both patients received intravenous steroids at high doses; in the first case, to manage a severe adverse event to the infusion of an EVD convalescent plasma,[2] and, in the second case, to treat a thrombocytopenic febrile syndrome with diffuse lymphadenopathy and pericardial effusion. Both patients fully recovered at discharge and no clinical sequelae at months 13 and 7 of follow-up were reported, respectively.

Use of corticosteroids in acute severe infectious diseases has been well documented.[3,4] Tuberculosis and cryptococcal meningitis, immune reconstitution inflammatory syndromes, and severe community-acquired pneumonia are all diseases with evidence that favours the use of steroids. Additionally, experience with another virus with haemorrhagic expression, the Puumalavirus, documented an excellent outcome in a few patients with multiorgan failure treated with an aggressive approach that included the use of steroids.[5]

As suggested by Hunt and Knott,[6] knowledge of a likely exposure to steroids during the EVD acute phase in the Sierra Leone cohort could be of great interest. Apart from anecdotal cases, only a systematic collection of epidemiological and clinical data from large EVD patient cohorts could provide unequivocal evidence on the impact of steroid use on the occurrence of clinical sequelae after Ebola virus infection.

We declare no competing interests. We received funding from Ricerca Corrente Italian Ministry of Health.

*Emanuele Nicastri, Nicola Petrosillo, Francesco Vairo, Antonino Di Caro, Giuseppe Ippolito
emanuele.nicastri@inmi.it

National Institute for Infectious Diseases (INMI), Lazzaro Spallanzani IRCCS, Via Portuense 292, 00149 Rome, Italy

1 Mattia JG, Vandy MJ, Chang JC, et al. Early clinical sequelae of Ebola virus disease in Sierra Leone: a cross-sectional study. *Lancet Infect Dis* 2016; **16:** 331–38.
2 Petrosillo N, Nicastri E, Lanini S, et al. Ebola virus disease complicated with viral interstitial pneumonia: a case report. *BMC Infect Dis* 2015; **15:** 432.
3 Critchley JA, Young F, Orton L, Garner P. Corticosteroids for prevention of mortality in people with tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis* 2013; **13:** 223–37.
4 Siemieniuk RAC, Maureen OM, Alonso-Coello P, et al. Corticosteroid therapy for patients hospitalized with community-acquired pneumonia. A systematic review and meta-analysis. *Ann Intern Med* 2015; **163:** 519–28.
5 Seitsonen E, Hynninen M, Kolho E, Kallio-Kokko H, Pettilä V. Corticosteroids combined with continuous veno-venous hemodiafiltration for treatment of hantavirus pulmonary syndrome caused by Puumala virus infection. *Eur J Clin Microbiol Infect Dis* 2006; **25:** 261–66.
6 Hunt L, Knott V. Serious and common sequelae after Ebola virus infection. *Lancet Infect Dis* 2016; **16:** 270–71.