Authors' Reply

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EVIDENCE FROM A VARIETY OF SOURCES indicates that the term "chronic Lyme disease" is a misnomer and is often improperly used to diagnose patients who have illnesses completely unrelated to *Borrelia burgdorferi* infection.¹⁻⁴ Our study found that patients with chronic Lyme disease were significantly more likely to be female than were patients reported to the Centers for Disease Control and Prevention (CDC) with Lyme disease (odds ratio [OR] = 2.42, 95% CI 1.98-2.94, $p < 0.0001$) or than were those with "post-Lyme disease syndrome" (OR = 2.32, 95% CI 1.62-3.34, $p < 0.0001$).⁵ These results suggested the likelihood that nonspecific illnesses with a female predominance, such as fibromyalgia, are being misdiagnosed as chronic Lyme disease.⁵⁻¹¹ A recent publication by Hassett et al.¹² corroborates both the findings and the conclusions of our report. Using patients evaluated at an academic Lyme disease referral center in New Jersey, these investigators distinguished patients with chronic Lyme disease from those with post-Lyme disease syndrome or active Lyme disease. Of the 46 patients categorized as having chronic Lyme disease, 38 (82.6%) were female compared with 17 (54.8%) of the 31 with post-Lyme disease syndrome ($p = 0.01$) and with 20 (50%) of the 40 with active Lyme disease ($p = 0.002$). Consistent with the observed difference in gender, patients with chronic Lyme disease were significantly more likely to be diagnosed with fibromyalgia than were those with post-Lyme disease syndrome (60.9% vs. 25.8%, $p = 0.003$).

In their letter, Stricker and Johnson¹³ hypothesize that the reason for the male predominance in Lyme disease is that the evidence-based interpretative criteria for immunoblot testing recommended by the CDC are in some way biased against women. This is a specious argument for many reasons. First, a recent study explicitly demonstrated that there is no effect of gender on the results of serological testing for Lyme disease.¹⁴ Moreover, to our knowledge, gender bias in serological testing for infectious diseases is unprecedented. Second, Stricker and Johnson appear to have overlooked the fact that >70% of Lyme disease cases reported to the CDC are based on the occurrence of erythema migrans (EM) only and, thus, are unrelated to any immunoblot result.¹⁵ Considering only patients with EM, there is still a male predominance in reported cases (Paul Mead, CDC, personal communication, 2009). A similar male predominance is seen in a wide variety of other tick-borne and mosquito-borne diseases,¹⁶⁻¹⁹ consistent with an increased risk of exposure to arthropod bites among men.

In addition, in contrast to what Stricker and Johnson state, seropositivity was not in fact a requirement in the Krupp et al. study²⁰ or in one of the two Klempner et al.²¹ trials.

Contrary to what Stricker and Johnson assert,¹³ evidence convincingly shows that the alternative immunoblot criteria used by Donta^{22,23} to diagnose chronic Lyme disease are insufficiently specific to be useful clinically.¹ Furthermore, the putative relationship of a decrease in CD57 natural killer cells to post-Lyme disease symptoms has been shown to be invalid.²⁴

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Disclosure Statement

The authors have no conflicts of interest to report.

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