

agnosed in patients with Lyme disease, which is caused by intracellular *Borrelia* infections.<sup>2</sup> In addition, patients with chronic fatigue may have intracellular *Chlamydia* spp. or mycoplasmal infections. Brucellosis and tuberculosis are also important causes of chronic fatigue.<sup>3</sup>

Patients with symptoms of fatigue should be screened for these bacterial infections.

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Thanks to Jacques Cornuz and colleagues<sup>1</sup> for reporting the case of fatigue in primary care. Studies here in Australia have highlighted the need for a thorough history and targeted laboratory testing, although most test results will be "normal."<sup>2</sup>

I am interested in what happened next in this case. The woman had laboratory features for celiac disease, but was this the cause of her symptoms? After the biopsy, did she start a gluten-free diet and then undergo another biopsy? Did she feel better on a gluten-free diet? If not, then we still do not have an adequate explanation for her symptoms. We, the physicians, have "treated" ourselves but not the patient.

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#### [The authors respond:]

We agree with Riccardo Baschetti that hypocortisolism is one of the reported laboratory abnormalities of patients with chronic fatigue syndrome and that hypoactivity of the hypothalamic-pituitary-adrenal axis is a potential pathophysiologic mechanism. However, as recently stressed by Cho and colleagues,<sup>1</sup> the question of whether such hypoactivity is a cause or a consequence of chronic fatigue syndrome remains unanswered. Our review<sup>2</sup> was intended to cover the diagnostic approach to chronic fatigue, rather than treatment, but we can mention here that the results of trials evaluating hydrocortisone therapy have been inconsistent. The first trial assessing this pharmaceutical approach<sup>3</sup> showed only a modest benefit at the expense of adrenal suppression. To our knowledge, the promising results of a second randomized trial assessing lower dose<sup>4</sup> have never been replicated.

As noted by Prasanta Padhan, the workup for chronic fatigue should be adapted to the local context according to the prevalence of diseases causing fatigue, including bacterial infections. Fatigue has been described in both early and chronic Lyme borreliosis. In one prospective study, fatigue was present in more than half of patients with early Lyme disease, and fatigue was more frequent than arthralgia, myalgia or headache.<sup>5</sup> In addition, Lyme disease may lead to a post-Lyme borreliosis syndrome including fatigue.<sup>6</sup> However, the appropriateness of serological testing depends on the probability of disease. Although such testing would be appropriate for a patient with fatigue and a history of erythema migrans (i.e., high pretest probability), it could be inappropriate for a patient suffering fatigue with no objective signs (i.e., low pretest probability) because of the high risk of false-positive results.<sup>7</sup> The pretest probability should also be considered for brucellosis and tuberculosis testing. *Chlamydia* and

*Mycoplasma* have been found in patients with chronic fatigue and might be associated with the severity of symptoms.<sup>8</sup>

David Barton is correct that most test results for patients with fatigue will be normal, and we agree that physicians must avoid performing diagnostic procedures simply to address their anxiety about a lack of diagnosis. Because our teaching case report represented an amalgamation of cases, there is no follow-up information. However, in a trial involving women with fatigue<sup>9</sup> (on which one of us [B.F.] was a coauthor) celiac disease was diagnosed by serologic testing and then small-intestine biopsy in 2 patients. One of these patients was lost during follow-up but the other undertook a gluten-free diet and was followed clinically after diagnosis for 12 months. After a few months, she felt better and her fatigue subsided. She underwent a second biopsy 12 months after the diagnosis, which showed no histologic abnormalities.

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