strongly suggest that applying our strategy of using the QFT-GIT test in the tuberculosis household contact investigation in areas with high prevalence of NTM would reduce the number of preventive treatments even further. However, it should be kept in mind that the safety of this strategy has been proved only for screening immunocompetent persons with the QFT-GIT test, and presumably with the new-generation QuantiFERON-TB Gold Plus test.

Note

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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C-Reactive Protein Response in Patients With Post-Treatment Lyme Disease Symptoms Versus Those With Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

To the Editor—There is substantial overlap in symptoms, including fatigue, muscle and joint pain, and cognitive and memory deficits, between post-treatment Lyme disease syndrome (PTLDS) and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) [1]. Increasing evidence suggests a role for immunologic and inflammatory pathways in both PTLDS and ME/CFS [2–4]. However, in part owing to their etiologic complexity and the lack of established biomarkers, our understanding of the pathways involved and potential mechanistic differences between the 2 conditions is very limited.

In a 2016 study published in *Clinical Infectious Diseases,* Uhde et al [5] examined the concentrations of acute-phase response proteins, including C-reactive protein (CRP), in individuals with PTLDS. CRP is a highly sensitive marker of infection and inflammation that binds a variety of ligands present on the surface of pathogens or exposed during autologous cell stress or death, exerting its effect through opsonin deposition and activation of the complement pathway, in addition to direct interaction with phagocytic cells [6]. We found that the circulating levels of CRP, as well as the frequency of concentrations >3 mg/mL (generally considered to represent some degree of inflammation [7]) to be significantly higher in the PTLDS cohort than in a control group of subjects who had a history of Lyme disease but without persistent symptoms (both $P < .001$). The data provided evidence for increased expression of an objective marker of inflammation in PTLDS but suggested a mechanism of activation distinct from that in active infection, as previously discussed [5].

Using the same methods [5] in a new study, we screened plasma samples from 131 patients with ME/CFS (89 female; mean age [standard deviation], 50.0 [11.4] years; mean body mass index (BMI), 26.0 [5.5]) and 86 healthy controls (68 female; mean age, 50.0 [12.8] years; mean BMI, 26.5 [6.8]), provided by the SolveCFS BioBank [8]. Patients with ME/CFS met the criteria of Fukuda et al [9] and the Canadian criteria [10] for this condition [9, 10]. Screening questionnaires were used to evaluate the general health of the unaffected controls and to confirm that they did not meet ME/CFS case definition criteria. The ME/CFS and control sample sizes provided >95% power, with an α value <.05, to detect the same increase in CRP response as in the patients with PTLDS [5]. Group differences were assessed by the analysis of covariance, using the general linear model, to account for the potential confounding effect of age, sex, and BMI. This study was approved by the Institutional Review Board of Columbia University. In contrast to data from patients with PTLDS [5], we did not find a statistically significant difference in the circulating levels of CRP (Figure 1) or the frequency of CRP levels >3 mg/L (33 of 131 [25.2%] vs 22 of 86 [25.6%], respectively) between patients with ME/CFS and controls.

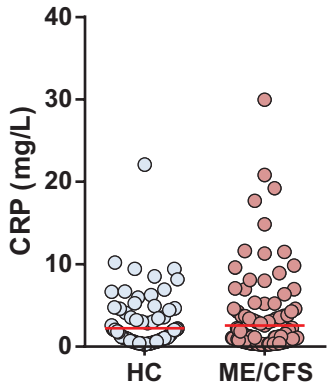

Figure 1. C-reactive protein (CRP) concentrations in the cohorts of patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and healthy controls (HCs). The difference between the 2 groups was not statistically significant ($P = .55$). Horizontal red bars represent the mean for each group.

These data provide evidence for the likely existence of distinct inflammatory mechanisms in ME/CFS versus PTLDS, which may be driven in part by the potentially more heterogeneous etiology of ME/CFS symptoms in comparison with PTLDS. The absence of a significantly enhanced CRP response in ME/CFS, despite published data suggesting activation of various inflammatory pathways, warrants further examination.

Notes

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No Impact of Hepatitis B Virus Infection on Early Mortality Among Human Immunodeficiency Virus–Infected Patients in Southern Africa

To the Editor—We read with interest the informative article by Kouamé et al describing mortality in human immunodeficiency virus (HIV)/hepatitis B virus (HBV)-coinfected patients on antiretroviral therapy (ART) in West Africa [1]. In line with studies from high-income countries, the results from the Temprano trial show that active HBV infection increases mortality among HIV-infected individuals [2]. However, clinical trial data cannot be generalized to other clinical settings in sub-Saharan Africa (SSA), where resources for patient monitoring and management are limited and patients who initiate ART often present with advanced stages of disease. Real-life data on the impact of HBV determinants on mortality from primary HIV care settings in SSA are scarce.

Since January 2013, we recruited consecutive HIV-infected patients at time of ART initiation into a prospective cohort in Lusaka, Zambia, and Ancuabe, a rural area in Mozambique, within the IeDEA collaboration [3]. All patients were tested for the presence of chronic HBV infection, defined as a positive HBsAg rapid test (Determine®, Alere, Yavne, Israel), and HBV viral load (VL) was measured in HIV/HBV-coinfected individuals using quantitative real-time polymerase chain reaction (Roche, Indianapolis, Indiana) from plasma or dried blood spots [4]. The systematic tracing of patients lost to follow-up (LTFU; i.e., >3 months without a clinical visit) during the first year of ART was performed by phone calls or home visits. We used multivariable Cox proportional hazards methods to compare 1-year mortality between HBV-infected and uninfected patients.

Fourteen percent (276/1948) of the study participants were HBsAg-positive, of whom 137 (49.6%) had an HBV VL above 2000 IU/mL. Median age was 32 years (interquartile range [IQR] 26–40 years), median CD4 count 252 cells/μL (IQR 130–369), 38% had World Health Organization (WHO) stage 3 or 4, and 36% were female. There were no significant differences in CD4 cell counts, body mass index, age, and proportions with advanced HIV disease between groups. HBsAg-positive individuals were more likely to be male ($P < .001$). After 1 year of ART, 129 (6.6%) patients had died, 113 (5.8%) were LTFU, and 63 (3.2%) transferred or withdrew from the study. One-year mortality was 6.5% (95% confidence interval 5.4–7.8%) in HIV-infected patients, 8.7% (4.9–15.2%) in HIV/HBV-coinfected with HBV VL <2000 IU/mL, and 8.2% (95% CI 4.4–15.2%) in HIV/HBV-coinfected patients with HBV VL >2000 IU/mL. In multivariable analyses, HBsAg-positivity was not associated with mortality (Table 1).

As opposed to Kouamé et al, we did not find a significant difference in mortality between HIV-infected individuals with active HBV infection and HBV-uninfected ones in southern Africa. We provide robust mortality estimates from primary care clinical settings in SSA, as we limited the risk of underestimating death rates by systematically tracing