To the Editor—We appreciated the recent study by Masson et al that utilized multiplex bead-based enzyme-linked immunosorbent assays (MBB-ELISAs) to associate human immunodeficiency virus (HIV) seroconversion with raised genital inflammatory cytokines from samples from cervicovaginal lavages from KwaZulu-Natal, South Africa [1]. The authors found that several cytokines, including macrophage inflammatory protein 1B, macrophage inflammatory protein 1A, interferon gamma-induced protein 10, interleukin 8 levels, were elevated in HIV seroconverters compared with non-converters. We conducted a pilot study using MBB-ELISAs to simultaneously screen for 63 cytokines in sera samples collected from patients with and without syphilis in Lima, Peru. Interestingly our study found elevated levels of similar chemotactic, inflammatory, and hematopoietic cytokines to the ones seen in the study by Masson et al.

We found 16 cytokines that were increased (P < 0.05) in 5 HIV–antibody negative, syphilis-infected (rapid plasma reagin [RPR] ≥ 1:32, treponema pallidum particle agglutination assay [TPPA]-positive) participants (average age: 32 ± 8.8 years) and 5 HIV–antibody negative, syphilis-negative (RPR non-reactive, TPPA-negative) participants (average age: 35.6 ± 7.9 years). Of those 16 cytokines, 11 were not previously described in the literature as being syphilis associated: interleukin 7 (P = .01), vascular endothelial growth factor D (P = .01), macrophage inflammatory protein 1B (P = .01), interferon gamma-induced protein 10 (P = .02), interleukin 12 active heterodimer (P = .02), leptin (P = .02), monocyte-specific chemokine 3 (P = .02), nerve growth factor (P = .03), eotaxin (P = .04), granulocyte macrophage colony-stimulating factor (P = .04), and platelet-derived growth factor (P = .04) [2–10]. We found increased median fluorescence intensity (MFI) values for all of the 16 cytokines in

Figure 1. Cytokine log-transformed median fluorescence intensity (MFI) values with significant differences between specimens from active syphilis case subjects compared with syphilis-negative control subjects. Abbreviations: GMCSF, granulocyte macrophage colony-stimulating factor; IL, interleukin; IP10, interferon gamma-induced protein 10; MCP3, monocyte-specific chemokine 3; MIP1B, macrophage inflammatory protein 1B; NGF, nerve growth factor; PDGFBB, platelet-derived growth factor BB; TNFA, tumor necrosis factor alpha; VEGF, vascular endothelial growth factor; VEGFD, vascular endothelial growth factor D.
specimens from syphilis case subjects except for eotaxin, which had a decreased MFI among syphilis case subjects compared with specimens from participants without syphilis (see Figure 1). The cytokines that were elevated in both Masson et al and our study include macrophage inflammatory protein 1B and interferon gamma-induced protein 10.

Our pilot study found at least 11 previously unidentified cytokines associated with active syphilis infection. Those previously unidentified cytokines give an indication that there still may be other undiscovered cytokines associated with syphilis that could be used to better understand the pathogenesis of the disease and may play a role in future diagnostic testing. We are planning longitudinal studies and studies with larger sample sizes to confirm our findings and conduct analyses using groups of cytokines. Masson et al postulate that susceptibility of HIV infection is associated with elevated genital inflammatory cytokines. From our data that show that syphilis infection causes elevations in sera samples of similar chemotactic, inflammatory, and hematopoietic cytokines as the ones that Masson et al observed, future research should be done to look at the impact of syphilis infections on elevations in genital inflammatory cytokines.

**Note**

**Potential conflicts of interest.** All authors: No potential 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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