Syphilis, while curable, may present either with symptoms or without symptoms. Distinguishing between active versus treated infection can be difficult in the asymptomatic stage.

New tests formulated on the basis of a host cellular response may allow for the differentiation of active or treated infection. Prior studies have linked certain cytokines with active infection using transcriptional profiles or single cytokine assays.

Objectives

- To better understand the pathogenesis of syphilis by investigating sera cytokine levels in men infected with syphilis.
- To explore cytokine markers of syphilis.

Aim

We aimed to simultaneously measure 63 cytokines from clinical specimens from men who were infected with syphilis.

Methods

The study was conducted at two sexual health clinics, Epicentro and Barton HealthCenters in Lima, Peru.

Participants

Sera were collected from 5 HIV-negative individuals infected with syphilis (rapid plasma reagent titer $\leq 32$, Treponema pallidum particle agglutination assay positive, mean age 32 ± 8.8 years), and 5 HIV-negative, syphilis-negative (negative serologic tests, mean age 35.6 ± 7.9 years).

Experimental procedure

Using a multiplex bead-based enzyme-linked immunosorbent assay, we conducted a pilot study comparing the median fluorescence intensity (MFI) of 63 cytokines in the sera specimens.

MFI values between groups were compared using a Wilcoxon rank-sum test.

P-value of <$0.05$ was considered statistically significant.

Ethics statement

Institutional review boards at Universidade Peruana Cayetano Heredia and Barton Health Center approved the study protocol. All participants gave written informed consent for participation.

### Results

We identified significant differences in 16 cytokines between groups. Of those cytokines, 8 were not previously described in the literature: interleukin 7, interferon gamma-induced protein 10, leptin, monocye-specific chemokine 3, nerve growth factor, eotaxin, granulocyte macrophage colony-stimulating factor, and platelet-derived growth factor.

Cytokines associated with syphilis could be used to better understand the pathogenesis of the disease and may play a role in future diagnostic testing.

### Discussion

Our pilot study found at least eight previously unidentified cytokines associated with active-syphilis infection. Longitudinal studies and studies with larger sample sizes are needed to confirm our findings and conduct analyses using groups of cytokines.

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