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Neisseria gonorrhoeae cervicitis and human immunodeficiency virus (HIV) type 1 frequently coinfect core transmitter populations, such as female sex workers. Gonococcal cervicitis is associated with increased viral shedding and plasma viremia in HIV-1-infected women and increased HIV-1 susceptibility in uninfected women. We studied the influence of gonococcal cervicitis on CD8(+) interferon (IFN)-gamma responses to HIV-1 and cytomegalovirus (CMV) epitopes in HIV-1-infected and in highly-exposed, persistently seronegative (HEPS) female sex workers. In HIV-1-infected women, gonococcal cervicitis was associated with reduced IFN-gamma responses in bulk CD8(+) lymphocyte populations, and intracellular cytokine staining, combined with class I major histocompatibility complex (MHC)-peptide tetramer studies, demonstrated reduced IFN-gamma production by HIV-1 epitope-specific CD8(+) lymphocytes. In HEPS sex workers, cervicitis was associated with the transient loss of systemic HIV-1-specific CD8(+) responses and with reduced function of CMV-specific CD8(+) lymphocytes. Impaired function of virus-specific CD8(+) lymphocytes may partly explain the deleterious effects of gonococcal cervicitis on HIV-1 immune control and susceptibility.