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**BACKGROUND AND OBJECTIVES:** Genital ulcer disease (GUD) is a major risk factor for human immunodeficiency virus (HIV) transmission. Cross-sectional studies have suggested that HIV infection may itself predispose to genital ulceration (GU). GOAL: To prospectively study the effects of HIV type 1 (HIV-1) infection and behavioral variables on GU incidence. METHODS: A cohort of 302 Kenyan female sex-workers was established in April 1991. Women were scheduled for assessment every 2 weeks, and bloods were collected every 6 months for HIV serology, rapid plasma reagin (RPR) and CD4 counts. Logistic regression was used to study risk factors for incident genital ulcers. **RESULTS**: 189 women (62.5%) had at least one incident ulcer over 24.3 +/- 15.3 months. GU incidence was higher in seropositive than initially seronegative women (82% vs. 48%; odds ratio [OR]) = 4.33; P < 0.01). Only HIV-1 seropositivity (OR = 3.42), a CD4 count < 200/ml (OR = 1.94), and oral contraceptive use (OR = 1.35) were associated (P < 0.05) with GU incidence in regression analysis. For those ulcers where an etiology was actively sought, Hemophilus ducreyi was confirmed in 54 (19%) of cases, and syphilis in 30 (29%). CONCLUSION: GU incidence in Kenyan sex workers is independently affected by HIV-1 serostatus, degree of immunosuppression, and oral contraceptive use.