

SCREENING FOR ANAL SQUAMOUS INTRAEPITHELIAL LESIONS

A meta-analysis estimated the clinical benefits and cost-effectiveness of screening HIV-positive homosexual and bisexual men for anal squamous intraepithelial lesions (ASIL) and anal squamous cell carcinoma. Researchers calculated lifetime costs, life expectancy, and quality-adjusted life expectancy for no screening and four screening strategies using anal Papanicolaou (Pap) tests (screening every 3 years, every 2 years, every year, and every 6 months). In patients with CD4 cell counts higher than $0.5 \times 10^9/L$, anal Pap screening every 2 years increased quality-adjusted life expectancy by 2.7 months and increased total costs by \$2940, resulting in an incremental cost-effectiveness ratio of \$13,000 per quality-adjusted life year (QALY) saved compared with no screening. Annual Pap screening demonstrated a clinical benefit of \$16,600 per QALY saved compared with screening every 2 years. In patients with CD4 cell counts lower than $0.5 \times 10^9/L$, annual anal Pap screening demonstrated a clinical benefit of less than \$25,000 per QALY saved compared with no screening. Increasing screening frequency to every 6 months did not demonstrate significant clinical benefit in either patient population when compared with annual screening. The study concluded that screening HIV-positive homosexual and bisexual men for ASIL was associated with substantial benefit, regardless of HIV development. Additional research is necessary to identify rates of progression of high-grade ASIL to cancer with and without highly active antiretroviral therapy, to evaluate treatment modalities for high-grade ASIL, and to assess acceptability of screening to both patients and health care providers.

Goldie SJ, Kuntz KM, Weinstein MC, et al: The clinical effectiveness and cost-effectiveness of screening for anal squamous intraepithelial lesions in homosexual and bisexual HIV-positive men. JAMA 1999;281:1822-1828.

HIV-1 REPLICATION AFTER COMBINATION ANTIRETROVIRAL THERAPY

A cohort study examined evidence of ongoing HIV-1 replication as well as a decrease in the size of the latent reservoir in patients who had undetectable plasma HIV-1 RNA levels for 2 to 3 years during combination therapy with three or four drugs. The study included patients ($n = 8$) who exhibited complete suppression of plasma HIV-1 while being fully compliant with the prescribed antiretroviral therapy. Sequential peripheral-blood mononuclear cells (four from each patient) were examined for changes in DNA sequence, which would indicate ongoing replication of HIV-1. No evolution of viral sequence was demonstrated during treatment in six of the eight patients.

However, two patients exhibited substantial sequence divergence only possible through continued viral replication. Despite viral replication, no evidence of drug-resistant viral genotypes was found in the DNA of these patients. Ongoing HIV-1 replication was demonstrated in the lymphocyte population of one of the patients with sequence divergence. The study concluded that highly active antiretroviral therapy is not always strong enough to eradicate HIV-1 infection or induce remission. Continued research is necessary to facilitate a truly effective therapy able to eliminate the latent reservoir of HIV-1.

Zhang L, Ramratnam B, Tenner-Racz K, et al: Quantifying residual HIV-1 replication in patients receiving combination antiretroviral therapy. N Engl J Med 1999;340:1605-1612.

ACQUIRED RIFAMYCIN MONORESISTANCE

Researchers examined a randomized, open-label multicenter study comparing two regimens of short-course tuberculosis therapy to determine possible mechanisms of acquired rifamycin monoresistance in HIV-seropositive patients. Patients with HIV-related tuberculosis (an HIV-seropositive group and an HIV-seronegative group) were randomized to rifapentine and isoniazid once weekly or rifampin and isoniazid twice weekly for the last 4 months of standard 6-month tuberculosis therapy. Within the observation period, four HIV-seropositive patients in the rifapentine/isoniazid arm developed rifamycin monoresistance, which led to the premature closure of the HIV-seropositive study group. Patients in the HIV-seropositive group ($n = 61$) were assessed for tuberculosis relapse. No treatment failures occurred during the study phase. Five of 30 patients in the rifapentine/isoniazid arm and three of 31 patients in the rifampin/isoniazid arm relapsed after treatment. The relapses in the rifapentine/isoniazid arm occurred from 9 to 34 weeks after treatment ended; the relapses in the rifampin/isoniazid arm occurred from 11 to 24 weeks after treatment. Age, CD4 cell count, combined extrapulmonary and pulmonary disease at baseline, and use of azole antifungal drugs each demonstrated a univariate association with rifamycin monoresistant relapse. Researchers concluded that HIV-seropositive patients should not be treated with the once-weekly continuation-phase regimen of isoniazid and rifapentine.

Vernon A, Burman W, Benator D, et al: Acquired rifamycin monoresistance in patients with HIV-related tuberculosis treated with once-weekly rifapentine and isoniazid. Lancet 1999;353:1843-1846.

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