

PROTECTION AGAINST HIV TYPE 1 INFECTION IN PERSONS WITH REPEATED EXPOSURE

A cohort study examined the contribution of inherited versus acquired resistance to HIV-1 infection in 37 HIV-1-seronegative subjects who fit standardized criteria for repeated high-risk sexual exposure to HIV-1. Within the 2-year observation period, the study population frequently reported unprotected anal and/or vaginal intercourse with HIV-1-infected partners. Despite persistent high-risk sexual behavior, the subjects remained free of HIV-1 infection throughout the median study period of 23 months (range, 15 to 30 months). Analyses were performed to determine if inheritance of a defective CCR5 HIV-1 coreceptor was a correlate of resistance to HIV-1 in these subjects; however, frequency of the wild type, heterozygous, and homozygous genotypes was not statistically significant. HIV-1-specific immunity, rather than target cell resistance to infection, appeared to have the strongest correlation with protection from HIV-1 in the study group. The study concluded that HIV-negative persons who continue to practice high-risk sexual activities with an HIV-1-infected partner are more likely to be protected from infection through HIV-1-specific immunity rather than defective CCR5 HIV-1 coreceptor function.

Goh WC, Markee J, Akridge RE, et al: Protection against human immunodeficiency virus type 1 infection in persons with repeated exposure: evidence for T cell immunity in the absence of inherited CCR5 coreceptor defects. J Infect Dis 1999;179:548-557.

HIV-ASSOCIATED FEVER OF UNKNOWN ORIGIN

A retrospective case series described the clinical features of HIV-associated fever of unknown origin (FUO); 70 cases of FUO in 65 HIV-infected patients were examined. Criteria used to define HIV-associated FUO included: temperature greater than 101°F on multiple occasions; fever for more than 4 weeks' duration in outpatients or more than 3 days' duration in inpatients, including incubation of microbiological cultures for at least 2 days; and an uncertain diagnosis after 3 days of appropriate investigation. Appropriate investigation included determination of blood cell counts, liver enzyme tests, urinalysis, chest radiography, blood and urine cultures, and identification of localizing symptoms or specific findings on examination. The patient population included 54 men (88%) and 11 women (12%); mean (\pm SD) age was 36 ± 7 years (range, 21 to 52 years). The mean (\pm SD) CD4 cell count was $58 \pm 78/\text{mm}^3$ (range, 0 to $457/\text{mm}^3$). Seventy-one percent of the patients were receiving antiretroviral therapy and 78% were receiving prophylaxis against *Pneumocystis carinii* pneumonia. Most patients (99%) had been previously diagnosed with AIDS, and

the mean (\pm SD) duration of fever was 42 ± 52 days (range, 16 to 220 days). The etiology of HIV-associated FUO was established 72 times within the study population. Infectious diseases were the cause in 88% of the identified etiologies. Common diseases identified as causes of FUO included cytomegalovirus infection (11%), disseminated histoplasmosis (7%), and lymphoma (7%). Additional case series are necessary to assess the influence of antiretroviral agents and geographic location on HIV-associated FUO.

Armstrong WS, Katz JT, Kazanjian PH: Human immunodeficiency virus-associated fever of unknown origin: a study of 70 patients in the United States and review. Clin Infect Dis 1999;28:341-345.

COMBINATION ANTIRETROVIRAL THERAPY AND DECLINES IN AIDS INCIDENCE AND MORTALITY

A cohort study examined 622 HIV-positive homosexual and bisexual men with well-characterized dates of seroconversion to determine whether the 1996 declines in AIDS progression and AIDS-related mortality stem from changes in HIV incidence or increased use of combination antiretroviral therapy. Patients were interviewed at 6- to 12-month intervals. Study endpoints included current use of combination therapy with at least two antiretroviral drugs and/or protease inhibitors, AIDS diagnosis, and death. In the study sample, HIV seroconversions were highest in 1979 ($n = 184$); from 1980 to 1989, the number of seroconversions fell from 150 to 41. By the end of 1996, 505 patients were diagnosed with AIDS and 450 patients had died. AIDS incidence, which averaged 15.8 per 100 person-years from 1993 to 1995, peaked at 20.3 per 100 person-years in 1995 and dropped to 2.6 per 100 person-years in 1996. Mortality rates closely tracked AIDS incidence. Combination antiretroviral therapy with at least two drugs was reported by 22%, 13%, and 23% of study group patients in 1993, 1994, and 1995, respectively. Patients' use of antiretroviral therapy jumped to 49% and 79% in 1996 and 1997. Use of protease inhibitors increased from 4% of patients in 1995, to 61% in 1997. The study concluded that combination antiretroviral therapy has a measurable effect against AIDS progression and mortality and should be adopted as the current standard of care.

Vittinghoff E, Scheer S, O'Malley P, et al: Combination antiretroviral therapy and recent declines in AIDS incidence and mortality. J Infect Dis 1999;179:717-720.

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