Neopterin to Predict Disease Progression in Intravenous Drug Users Infected with HIV-1

R. ZANGERLE¹, D. FUCHS², G. REIBNEGGER³, P. FRITSCH³, H. WACHTER²

The AIDS Unit, Department of Dermatology and Venereology, ² Institute of Medical Chemistry and Biochemistry, University of Innsbruck, and ³ Ludwig Boltzmann Institute of AIDS Research, Innsbruck, Austria

Most of our knowledge about the natural history of HIV infection comes from cohorts of homosexual men and men with hemophilia. The natural history of Human Immunodeficiency Virus (HIV) infection in intravenous drug users (IVDUs) is different from other people at risk in as far as some diseases, such as bacterial pneumonia or endocarditis, contribute to morbidity and mortality (Moss 1989); however, these diseases related to drug intake are not listed in the existing HIV staging classifications nor in the AIDS definition. A staging system for HIV infection should be easily capable of determining individual prognosis for all people at risk, but such a system is still lacking (Chaisson 1990). Therefore, the identification of factors correlated with and possibly contributing to the outcome of infection with HIV is important for our understanding of the pathogenesis and natural history of HIV infection and in designing therapeutic trials. Many reports address the possibility of early prediction of HIV-1 related disease progression. Low numbers of CD4+ T cells and low ratios of CD4+/CD8+ T cells were shown to be associated with a more unfavourable disease course (Polk 1987, Moss 1988, Eyster 1989, Fahey 1990, Fernandez-Cruz 1990). Additionally, HIV-1 p24 antigenaemia (de Wolf 1988), increased concentrations of β2-microglobulin in serum (Moss 1988, Anderson 1990) and increased urinary and/or serum concentrations of neopterin
(Fahey 1990, Fuchs 1988, Fuchs 1989) indicated more rapid progression of the disease. However, the question remains whether these data, which were raised mainly from cohorts of homosexual men and men with haemophilia, also are valid for people with intravenous drug use. The aim of our study was to investigate the power of urinary neopterin to predict the development of AIDS or Walter Reed stage 5 (oral candidiasis in combination with a CD4 T cell count below $400 \times 10^{-6}$/liter).

**MATERIAL AND METHODS**

**Patients:** This retrospective study comprised a population of 47 IVDUs out of 121 HIV-1 infected IVDUs at our AIDS Outpatient clinic. The selection was made by the requirement of a complete clinical examination in combination with measurement of urinary neopterin and T cell subsets in 1989/1990, a follow-up of at least 3 months and absence of HIV-1 related symptoms at entry into the study. The mean observation period was 48 months (range 3-82 months). Mean age of the 30 men and 17 women was 25 years (range 18-36 years). All were persistent IVDUs and 16 were enrolled in late 1988 in the newly established methadone maintenance treatment programme (median duration of these participants in the programme was 11 months) and none of them received ziduvudine or inhaled pentamidine before the end point of the observation period, which was determined by either the last visit, or the development of AIDS, or diagnosis of oral candidiasis in combination with a CD4 T cell count below $400 \times 10^{-6}$/liter (WR 5). AIDS was diagnosed on the basis of the revised CDC definition of 1987 and oral candidiasis was diagnosed when in the presence of characteristic intraoral lesions, the examination of scrapings by potassium hydroxide revealed fungal forms. Other possible causes for the oral candidiasis were excluded in all patients. HIV-1 antibody status was determined by enzyme linked immunosorbenet assay (Abbott) and confirmed by Western blot analysis (DuPont) and was available at the initial visit. In some subjects the first HIV test was done with a sample from frozen serum stored before HIV testing was available.