

also believe there is substantial merit in evaluating the relative costs and benefits of alternative prophylaxis regimens. However, until we identify patients who do not derive sufficient benefit from prophylaxis to warrant its use, we believe that our results provide a better guide to practice than no data at all.

Boston, MA 02115
 Boston, MA 02215
 Boston, MA 02114
 Seattle, WA 98104
 Boston, MA 02115

RICHARD PLATT, M.D.
 Channing Laboratory

DORI F. ZALEZNIK, M.D.
 Beth Israel Hospital

CYRUS C. HOPKINS, M.D.
 Massachusetts General Hospital

E. PATCHEN DELLINGER, M.D.
 Harborview Medical Center

TOR D. TOSTESON, Sc.D.
 Channing Laboratory

MARKERS OF RISK IN HIV-1

To the Editor: Fahey et al. (Jan. 18 issue)¹ evaluated the usefulness of several serologic and cellular measures of immunity in predicting the onset of the acquired immunodeficiency syndrome (AIDS), using data on homosexual men infected with the human immunodeficiency virus (HIV) in the Multicenter AIDS Cohort Study (MACS). Because studies of prevalently positive subjects are potentially biased,² we report complementary data from a cohort with incident (i.e., dated) HIV infections followed annually for eight years.

Of 131 HIV-1-seropositive homosexual men evaluated approximately annually since 1982,³ 48 had AIDS by the end of 1988. The dates of seroconversion (the midpoint between the last negative and first positive samples) were available for 47 of the 131 men. For the 84 men already infected at the outset of the study, the seroconversion dates were estimated by the method of back-calculation to regional norms, according to which the men in New York were found on average to have seroconverted in June 1980, and those in Washington in June 1981.⁴ To check the reliability of this approach, we examined the annual and cumulative rates of AIDS incidence, using these derived seroconversion dates, and found them virtually identical to those with midpoint seroconversion dates.⁵

We evaluated the risk of AIDS on the basis of the proportion of CD4+ lymphocytes as determined by flow cytometry with OKT4 reagent (Ortho Diagnostics, Raritan, N.J.) and the serum levels of neopterin (Neopterin RIAcid, Henning-Berlin, Federal Republic of Germany) and β_2 -microglobulin (Beta-2-micro, RIA, Pharmacia, Uppsala, Sweden). The levels of β_2 -microglobulin and neopterin were more highly correlated (Spearman $r = 0.74$) than in the MACS results. When the test results in the first year after seroconversion were used, the incidence of AIDS at five years was strongly predicted by the proportion of CD4+ lymphocytes alone ($P = 0.001$): 15 of 29 men (52 percent) with a proportion of CD4+ lymphocytes below 25 percent had AIDS, as compared with 10 of 39 men (26 percent) who had a proportion of CD4+ lymphocytes from 25 to 35 percent and none of 12 men in whom this proportion was above 35 percent. The five-year rates of AIDS were also increased for those with high levels of β_2 -microglobulin (>3 mg per liter; $P = 0.01$) or neopterin (>15 nmol per liter; $P = 0.02$) in the first year after seroconversion. When a time-dependent covariate analysis^{5,6} was conducted, with the measurements grouped by terciles, the most predictive markers 2 to 12 months before the onset of AIDS were the combination of the proportion of CD4+ lymphocytes and the level of β_2 -microglobulin (relative hazard of AIDS, 8.0) or the level of β_2 -microglobulin alone (relative hazard, 5.0). AIDS was predicted two to three years before diagnosis by combined testing for the proportion of CD4+ lymphocytes plus either the β_2 -microglobulin or the neopterin level (relative hazard, 3.2 for each combination).

We conclude that serum levels of β_2 -microglobulin and neopterin may contribute to a more reliable prediction of AIDS risk than the

proportion of CD4+ lymphocytes alone. Such information can help guide the frequency of immunologic monitoring and direct effective forms of therapy such as zidovudine to those at highest risk. Moreover, the highest AIDS rates were in subjects who had seroconversions associated with marked declines in the proportion of CD4+ lymphocytes and marked elevations in the β_2 -microglobulin and neopterin levels. Understanding the pathogenesis of immunologically severe HIV seroconversions may provide therapeutic opportunities to reduce the risk of AIDS further.

D-7400 Tubingen,
 Federal Republic of Germany

ALEXANDER KRÄMER, M.D.
 Institute of Medical Biometry

ROBERT J. BIGGAR, M.D.
 JAMES J. GOEDERT, M.D.
 National Cancer Institute

Rockville, MD 20852

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ORGAN TRANSPLANTATION IN HIV-POSITIVE PATIENTS WITH HEMOPHILIA

To the Editor: An important question concerning transplantation is whether the subsequent survival and quality of life justify the procedure in HIV-infected patients. We reviewed or followed the course of five HIV-positive persons with hemophilia who underwent transplantation — four of a liver and one of a heart — between 1982 and 1987¹⁻⁴ (Table 1). All had asymptomatic HIV infection at the time of operation. Liver transplantation was performed in four patients because of end-stage liver disease due to long-term transfusion therapy, and heart transplantation was performed in one because of end-stage cardiomyopathy due to a thrombotic infarction that was complicating therapy with factor IX concentrate. One (Patient 1) died perioperatively of surgical complications and thus could not be evaluated. Of the four patients who could be evaluated, all survived transplantation but unfortunately went on to have AIDS 3, 14, 24, and 41 months later. Three have since died of complications of AIDS.

With respect to the quality of life before the development of AIDS, all but one patient had symptom-free survival after transplantation, resuming usual activities at school and work. The exception (Patient 4) had multiple bacterial infections, sepsis, and *Pneumocystis carinii* pneumonia within three months of transplantation. In another patient (Patient 5), lymphoproliferative lesions of the lung that occurred after transplantation resolved with a reduction of the cyclosporine dose. The only patient for whom zidovudine was available (Patient 3) was unable to tolerate the drug because of myelotoxicity associated with concomitant immunosuppressive therapy. The AIDS-free survival after transplantation, even despite immunosuppression, appeared to vary with the CD4 count at transplantation and varied inversely with the age at transplantation (Table 1), as has been observed in HIV-positive persons with hemophilia who did not undergo transplantation.⁵ However, survival after transplantation appears to be poorer than that described in published reports of transplant recipients who did not have hemophilia.⁶ This may relate to their longer duration of infection. Most HIV-positive persons with hemophilia have now been infected for