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Intravenous Dextran Sulfate (DS) Increases Circulating HIV Antigen Levels in Patients with ARC or AIDS. C. Flexner, P. Barditch-Crovo, D. M. Kornhauser, L. Nerhood, C. Hendrix, K. Lorentsen, H. Farzadegan*, B. G. Petty, and P. S. Lietman, Division of Clinical Pharmacology, The Johns Hopkins University School of Medicine, and * The Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland, USA.

Polysulfated polysaccharides have been proposed as potential antiviral drugs because of potent in vitro activity against HIV, herpesviruses, and other enveloped viruses. In order to investigate the potential anti-HIV activity of a prototypical polysulfated polysaccharide, we administered the maximally-tolerated dose of dextran sulfate (a continuous intravenous infusion adjusted to maintain an activated partial thromboplastin time [APTT] of 65 to 80 seconds [8 subjects] or 50 to 65 seconds [2 subjects]) to patients with ARC or AIDS for up to 14 days. Circulating HIV antigen (p24) levels increased significantly in all eight subjects receiving drug for six or more days (median proportional increase 73.5%, range 32-130%). This increase was highly significant when compared to a large cohort of untreated historical controls (Fisher's exact test, $p < .001$). DS infusion may have increased the production or reduced the clearance of virus or p24 protein. Attempts to uncover a methodological artifact have failed to explain this result. Plasma DS concentrations achieved with this protocol were 2.4 to 21.6 mcg/ml (median 6.8 mcg/ml), which are 20- to 200-fold greater than the in vitro IC_{50} for free HIV infectivity. Finally, the drug was toxic, producing profound but reversible thrombocytopenia in all subjects receiving drug for greater than three days, and extensive but reversible alopecia in five subjects. We feel that DS is unlikely to have a practical role in the treatment of symptomâtic HIV infection.

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Use of Flow Cytometry to Monitor the Expression of HIV p24 Antigen in PBMC Obtained from HIV-seropositive Individuals Undergoing Antiviral Chemotherapy. J McSharry, S Remick, S Szebenyi, D Herman, J Bills, J Slaga, P Gorman, A Ogden-McDonough, E Dickerson and J Lehman. Albany Medical College, Albany, New York, USA

A novel technique involving indirect immunofluorescence in conjunction with flow cytometry was developed to detect and quantitate the number of p24 antigen positive PBMC obtained from individuals infected with HIV (McSharry et al., J. Clin. Microbiol. 64:724, 1990). This procedure is rapid (24 to 48 hrs), sensitive and quantitative and the percent of p24 antigen positive PBMC reflects disease progression. This technique is being used to monitor the effect of antiviral chemotherapies, including ZDV, DDC and DDI, on the expression of p24 antigen in PBMC from AIDS patients. 25 patients have been entered on a double-blind comparative trial of ZDV vs DDC; 10 patients on a double-blind comparative trial of ZDV vs DDI; 4 patients on an open-label ZDV vs DDC comparative study; and another 193 patients are followed, the majority of whom are receiving ZDV off study. The median CD4 lymphocyte count at entry in these patients was 75 per ul (range 5-331 per ul). The median percent of p24 antigen positive PBMC at entry was 8.45% (range 4.5-18.6%). A patient is considered positive for p24 antigen employing this technique when greater than or equal to 4% of the PBMC are positive. Patients continue to be followed prospectively and this technique may be able to differentiate antiviral activity of the various nucleoside analogues currently under investigation. (Supported in part by NIH Grant # AI30883 and AmFAR Project Grant # 600027-9-CT).