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Ribavirin but not interferon protects against Pichinde' arenavirus infection. H. Lucia, D. H. Coppenhaver, T. Stevens, P. Sriyuktasuth, S. Baron. Department of Microbiology, University of Texas Medical Branch, Galveston, Texas, USA, 77550.

Pichinde', an arenavirus which has been adapted to strain 13 guinea pigs, causes a fatal hemorrhagic fever which can serve as a safe model of Lassa fever. We attempted antiviral therapy of Pichinde' infection in guinea pigs using guinea pig-active recombinant interferon (IFN) α A (Hoffman-LaRoche), the IFN inducing drug CL246,738 (Lederle), or ribavirin. IFN was not protective when administered intraperitoneally (10,000-30,000 IU) one hour before virus administration. Similarly, CL246,738 (5-15mg/kg, ip) given 24 hr before virus challenge did not exert any beneficial effect on the course of infection. In contrast, ribavirin (25 mg/kg/day, ip), given for 14 days starting on the day of infection, postponed the mean day of death from 14 to 22 days post infection. When ribavirin was administered daily for 28 days, minimal arenavirus symptoms were observed, and mortality was eliminated. These findings confirm the ineffectiveness of IFN and IFN inducers in treating arenavirus hemorrhagic fever. This study also demonstrates protection by ribavirin against Pichinde' virus, thus confirming the efficacy of ribavirin against arenavirus infections. Supported by USAMRIID contract #DAMD17-86-C-6119.

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Adverse Effects of Recombinant Human Tumor Necrosis Factor on the Course of Simian Varicella Virus Infection in Monkeys. K. F. Soike and C. W. Czarniecki, Delta Regional Primate Research Center, Covington, LA and Genentech, Inc., South San Francisco, CA.

Tumor necrosis factor α (TNF-α) is a multifunctional protein. It may exert a direct antiviral effect against some viruses and is cytolytic for some virus infected cells. We have attempted to evaluate the antiviral effects of recombinant human TNF-α in vivo in an animal model employing simian varicella virus (SVV) infection in African green monkeys. TNF-α was administered as twice daily i.v. injections at doses of 10, 3, or 1.0 μg/kg/day beginning 24 hours after virus inoculation. SVV infected monkeys treated with TNF-α developed more severe disease than infected untreated controls with marked viremia, high aminotransferase levels and early death. Histopathological examinations revealed more severe lesions in TNF-α treated monkeys than in controls. TNF-α administered to uninfected monkeys or to SVV-immune monkeys challenged with SVV showed no abnormalities or TNF-associated toxicity. The enhancement of disease parameters must therefore have resulted from the interaction of an active infection and the effects of TNF-α. The hypothesis that TNF-α enhanced SVV infection by its cytolytic effect on infected lymphocytes during viremia, thereby liberating larger quantities of virus could not be substantiated in vitro studies on SVV infected cells. The mechanism(s) leading to TNF-α enhanced disease is the subject of further work.