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Cellular and Humoral Factors Associated With Polyriboinosinic-Polyribocytidylic Acid (Poly I:C) Induced Resistance to Banzi Virus Encephalitis. D.C. Barnhart, E.P. Mayer, A. Ghaffar, and J.D. Gangemi, Department of Microbiology and Immunology, USC School of Medicine, Columbia, SC, 29208, USA.

A single intravenous dose of poly I:C (0.5 mg/kg) administered at the time of challenge with the flavivirus, Banzi, protected mice from lethal infection. In vivo treatment with antibodies to murine interferon-α, but not interferon-β, abolished the protective effects of poly I:C against Banzi virus. Thus resistance appeared to be mediated either by the direct antiviral properties of alpha interferon or by its influence on the antiviral functions of natural killer (NK) cells, T cells, and macrophages. To evaluate the significance of each of these cellular populations in enhanced resistance, a variety of selective depletion techniques were employed. Carrageenan (macrophage inhibitor) treated mice were fully protected from lethal virus infection by treatment with poly I:C. In addition, splenic macrophages, primed with poly I:C in vitro and adoptively transferred to untreated mice could not protect them from lethal Banzi virus encephalitis. Treatment with asialo GM1 antibody to eliminate NK cells did not diminish the protective effect of poly I:C in this model. Finally, the role of T cells was assessed in athymic (nu/nu) mice. No difference in protection was seen between nude mice and their normal littermates treated with poly I:C. These results provide evidence that the antiviral activity of poly I:C is mediated through the direct antiviral activity of alpha interferon.

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Comparison of the *in vivo* Anti-Punta Toro Virus Activity of Ribavirin, Ribavirin Triacetate and Ribamidine in Mice. J. H. Huffman, R. W. Sidwell, J. Gilbert, J. W. Huggins, and T. Monath. Utah State University, Dept. ADVS, Logan, UT 84322; and U.S. Army Medical Research Institute for Infectious Diseases, Frederick, MD 21702-5011

Three related compounds, ribavirin, ribavirin triacetate, and ribamidine, were examined in side-by-side experiments for efficacy against Punta Toro virus (PTV) infections in C57BL/6 mice. The toxicity, expressed as LD50, of each compound was determined when given to mice by either the s.c. or p.o. route of administration on a 2x/day for 5 days schedule. Doses of compounds, relatively equal by LD50 value, were used to determine relative antiviral efficacy by several parameters with changes in experimental procedures. Relative therapeutic indices (TI) of compounds administered either s.c. or i.p. were determined for virus titer in several tissues and for transaminase levels in serum. White blood cell counts were compared in mice treated by the p.o. route with different concentrations of the drugs. Effect of delaying initiation of 1x/day and 2x/day treatments for 5 days by either p.o. or s.c. administration was examined. The effect on number of survivors when the number of p.o. or s.c. treatments was reduced from 2x/day x 5 days to a single treatment. The influence of varying the virus challenge dose was compared when the compounds were given orally. The relative efficacy against daily development of disease parameters (death, liver score, transaminase levels, WBC counts, and virus titers in various tissues) was investigated when the compounds were given by a single LD50/16 oral dose. There were certain differences in individual compound activity seen in various experiments but none of the drugs had consistently better activity in all circumstances. Ribamidine was slightly better than the other two in controlling daily development of Punta Toro disease markers that were studied. [Supported by U.S. Army Medical Research Institute for Infectious Diseases Contract DAMD-86-C-6028].