152

Neurologic sequelae of experimental neonatal HSV-2 infection. FJ Bravo,[1] C Mani,[1] WS Ball,[1] CV Vorhees[1], LR Stanberry,[1] DI Bernstein,[2] MG Myers,[1] Children's Hospital and Research Foundation;[1] Cincinnati, OH, and the Gamble Inst. Med. Res.,[2] Cincinnati, OH.

Antivirals have reduced the morbidity and mortality of neonatal HSV-2 infection but some infants have longterm neurologic residua. Whether these are a consequence of initial infection, recurrences, or both is unresolved. Newborn guinea pigs inoculated with 3.3 $\log_{10}$ pfu HSV-2, MS strain, by corneal scarification develop neurologic signs, but recover, and survivors develop recurrent cutaneous lesions. In this study we evaluated MRI and auditory startle responses to assess the neurologic outcome of survivors of neonatal HSV-2 infection in guinea pigs.

Eleven uninfected and 20 infected animals were evaluated by magnetic resonance imaging (MRI) more than 3 weeks after inoculation. MRI revealed areas of low density in the paraventricular regions of the brain in 10 infected animals; 4 had no neurological symptoms initially.

Compared to 5 uninfected animals, 3 infected animals exhibited severely attenuated (90%) startle responses to both broad band mixed frequency signals and single frequencies ranging from 4-24KHZ. Infected animals exhibited weak prepulse startle inhibition and failed to show graded prepulse inhibition as a function of prepulse intensity. These findings may be due to impaired hearing in the infected animals and/or other damage of the startle reflex circuit.

Thus MRI and startle responses appear to provide means to assess the neurologic consequences of HSV infection in neonatal guinea pigs.

153

The SCID Mouse Model for Evaluation of Antiviral Agents Against Murine Cytomegalovirus (MCMV). D. F. Smee, J.L.B. Morris, J. R. Mead, and R. W. Sidwell. Antiviral Program, Department of Animal, Dairy and Veterinary Sciences, Utah State University, Logan, Utah, U.S.A. 84322-5600.

Severe combined immunodeficient (SCID) mice lack both T- and B-cell functions. They have been studied as models for AIDS virus infections. We have used SCID mice to study MCMV infections and to evaluate the effects of antiviral agents to combat the disease. SCID mice infected with extremely low doses of virus die from infection 14 to 21 days after virus challenge. These doses are 1000-fold lower than those required to kill normal BALB/c mice. Treatment with ganciclovir (25 mg/kg) for 10 day starting 24 hours after virus inoculation resulted in a delay in the time to death (by approximately 10 days), but the mice all died anyway. This is in contrast to the effects of ganciclovir in normal mice, who survive after cessation of antiviral treatment. Virus titers from organs and tissues were taken at three day intervals from 9 to 24 days after infection. Ganciclovir treatments suppressed MCMV titers during the treatment period, but titers rose after that as death approached. A recombinant human alpha A/D interferon preparation administered daily for 7 days and the interferon inducer bropirimine given every three days (treatment with each started 24 hours after virus challenge) failed to alter the course of MCMV disease progression. The SCID mouse model appears to more closely mimic human CMV infection in man than do other MCMV models, since disease progresses after discontinuation of ganciclovir treatment. This model should be useful for evaluating new antiviral agents and potentially active biological response modifiers.