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Capsaicin Reduces the Zosteriform Spread of Genital Herpes Simplex Virus Infection in Guinea Pigs. L.R. Stanberry, N. Bourne, F.J. Bravo, D.I. Bernstein. Children's Hospital Research Foundation, Cincinnati, Ohio, U.S.A.

The pathogenesis of HSV infections involves the transport of virus within peripheral nerves. Virus spread can be evaluated in animal models that exhibit a zosteriform distribution of cutaneous lesions because the secondary zosteriform lesions result from virus transported to and from dorsal root ganglia. We have previously described zosteriform spread of HSV-2 genital infection in male and female guinea pigs. Using these models we have explored the effect of capsaicin on HSV spread. Capsaicin, a compound with selective effects on sensory neurons, was administered to male or female Hartley guinea pigs by multiple subcutaneous injections over 2 days to a total dose of 125mg/kg. One day later animals were inoculated by application of HSV-2 to a scarified area on the left middle thigh. Control animals developed extensive zosteriform spread of lesions involving the leg, lower abdomen and genitalia (perineum including labia or penis). Capsaicin treated guinea pigs developed lesions at the site of inoculation but exhibited significantly less severe zosteriform spread of lesions ($p < .001$), suggesting that capsaicin-sensitive nerve fibers are involved in the spread of HSV. After recovery from primary infection male guinea pigs were evaluated daily from days 15-28 for evidence of recurrent herpetic lesions. Capsaicin treated male animals exhibited significantly fewer recurrences than controls ($p < .01$) suggesting that the pathogenesis of recurrent HSV infections also involves capsaicin sensitive neurons.

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The Effect of Age on the Outcome of Neonatal HSV Infection in Guinea Pigs. C. Mani, F.J. Bravo, L.R. Stanberry, M.G. Myers. Childrens Hospital Research Foundation, Cincinnati, OH.

HSV infection in newborn infants can be a devastating illness. To determine the effect of age on outcome of HSV illness in newborns, we randomized Hartley guinea pigs into 4 groups of 15 animals each. Group 1 were inoculated within 24 hours of birth, Group 2 were inoculated between 36-48 hours of age, Group 3 were inoculated at 7 days of life, and Group 4 were adult guinea pigs ($\geq$ 300 gms). Each animal was inoculated intranasally with 3.3 $\log_{10}$ pfu HSV-2, MS strain. Animals were examined daily to observe for signs of localized skin, eye, mouth (SEM) or disseminated disease and were assigned a severity score ranging from 0 to 4 with 1 point each awarded for skin lesions, ocular involvement, respiratory signs and neurologic findings. Tissues for culture and histology were obtained from animals that died. All but 1 adult animal developed SEM disease with onset between 2-6 days. The area under the severity score-day curves were (mean $\pm$ SEM): Group 1 = 17 $\pm$ 1.6; Group 2 = 20 $\pm$ 1.8; Group 3 = 13 $\pm$ 1.8; Group 4 = 10 $\pm$ 1.3. Mortality was affected by age at inoculation, being 100%, 73%, 46% and 13% in groups 1-4, respectively. All survivors developed spontaneous recurrent SEM lesions. The natural history of neonatal HSV-2 infection of guinea pigs is analogous to that which occurs in human infants. Outcome of caviid neonatal herpes is affected by age at inoculation. Although further study will be necessary to define those age dependent host factors that influence outcome of neonatal infection, this model offers great promise for the study of new antiviral strategies for the treatment of neonatal herpes.