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Immunoprophylactic Strategies for Prevention of Genital Herpes Simplex Virus Infections.

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Genital herpes simplex virus (HSV) infections continue to be a major health problem worldwide and although Acyclovir has been licensed for treatment of these infections for over 10 years, the incidence of genital herpes continues to increase. In an attempt to reduce or prevent transmission of genital HSV infections, we have utilized two Immunoprophylactic approaches in experimental genital HSV infections. For one strategy we treated groups of mice intravaginally (Ivg) with 900 or 300 μg of a monoclonal antibody (MAB) made against HSV-1 gB, 15, 30, or 60 minutes prior to Ivg infection with HSV-2. Mice treated with 900 μg of MAB 15 minutes prior to infection had reduced infection rates, reduced virus titers in vaginal tract and reduced mortality rates compared with placebo treated animals. For the second strategy, two avirulent deletion mutants of HSV that were capable of replicating in the nasopharynx and genital tract were used to infect mice by the intranasal or Ivg route. When these animals were challenged Ivg 21 days later with HSV, there was a significant reduction in mortality rates, but not in virus titers in vaginal tract, or infection rates compared with sham inoculated animals. In these experiments, antibodies administered passively Ivg reduced or prevented genital herpesvirus infections, whereas those induced by immunization with live virus did not alter infection rates or HSV replication in vaginal tract.

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Comparison of Penciclovir with Acyclovir for Treatment of Severe Herpes Simplex Virus Infections of Mice.

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Although treatment with Acyclovir (ACV) has reduced mortality and morbidity in patients with herpes encephalitis and neonatal herpes, therapy is still not optimal and additional treatment strategies are under investigation. Penciclovir (PCV), although closely related to ACV, has been reported to be phosphorylated more efficiently and have a much longer half life as the triphosphate than does ACV. To determine if PCV has superior activity to ACV, we compared both compounds in tissue culture and experimental infections in mice. In human foreskin fibroblast cells, PCV was 2-4 fold less active than ACV against a panel of Herpes Simplex Virus Type 1 and Type 2 (HSV-1, HSV-2) isolates. In groups of mice inoculated intranasally with HSV-1, a model of herpes encephalitis, treatment with 40 mg/kg of PCV significantly reduced mortality when initiated 72h after infection. Similar levels of protection were obtained with 10-20 mg/kg of ACV. In mice treated with the same concentration of each drug, ACV more effectively reduced HSV-1 replication in brain tissue than did PCV. When mice were inoculated intranasally with HSV-2, a model of neonatal herpes, significant protection was obtained at 20-40 mg/kg of PCV and 40 mg/kg of ACV. In this model infection, treatment with ACV also appeared to more effectively inhibit HSV-2 replication in brain and lung than PCV. In our studies, PCV is 2-4 fold less active in tissue culture than ACV and in two experimental HSV infections in mice PCV was generally about 2-fold less active in reducing final mortality rates and HSV replication in target organs.