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Effect of Indomethacin on UV-induced recurrent genital HSV-2 disease in the guinea pig. C. J. Harrison[1], D. F. Bratcher[1], N. Bourne[1], L.R. Stanberry[1], and D.I. Bernstein[2], Children's Hosp. Res. Fnd.[1] and the Gamble Inst. Med. Res.[2], Cincinnati, Ohio.

We have shown that recurrent genital herpes simplex virus (HSV) disease can be induced in latently infected guinea pigs by ultraviolet (UV) irradiation. Previous studies have demonstrated that UV radiation exposure is associated with local increases in prostaglandin activity. We therefore studied the effects of indomethacin (IND), a prostaglandin inhibitor, on UV induced reactivation of HSV. Primary genital infection was produced in 26 Hartley guinea pigs by intravaginal inoculation with 5 X 10^5 pfu/ml HSV-2 strain 333. On day 100 post-inoculation, animals were randomized into two 5-day treatment groups (intramuscular IND at 10 mg/kg, or an equivalent volume of saline). On day 101, metaphane anesthetized animals were exposed to 10 min of UV-B light produced by transilluminators emitting radiation between 280-320 nm with a peak output of 7000 uW/cm^2 at 302 nm. Animals were scored for recurrences over the next 7 days. The IND-treated group had fewer total lesion days than the placebo group (25 vs. 3). Only 2/13 animals in the IND-treated group developed recurrent lesions compared to 11/13 animals in the placebo recipients, $p<0.002$. Severe recurrent disease (more than one concurrent vesicle) occurred only in the placebo group. Mean lesion days/animal for the 7 day observation period were 0.20 ± 0.15 for placebo vs 0.02 ± 0.07 for IND recipients, $p<0.001$. In this study, systemically administered IND reduced the incidence of UV-induced recurrent disease in the guinea pig model.

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Effect of Topical Treatment with HPMPC on Genital Herpes Simplex Virus Type 2 (HSV-2) Infections of Guinea Pigs or Mice.

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The Nucleoside Analogue (S)-1-(3-Hydroxy-2-Phosphonylmethoxypropyl) Cytosine (HPMPC) has been shown to be very active against HSV-1 or HSV-2 both in vitro and in vivo. The replication of HSV-1 or HSV-2 in tissue culture cells is inhibited by about 1.0 μg/ml of HPMPC, whereas Acyclovir (ACV) has an ED_{50} of about 0.10-0.50 μg/ml. The purpose of these studies was to evaluate the efficacy of topically applied HPMPC in animal models of primary genital HSV-2 infections. In guinea pigs, previous studies indicated toxicity with 5% HPMPC so treatment with 1% or 0.3% HPMPC three times daily or once daily was initiated 24 or 72H post inoculation. Therapy with 1% HPMPC beginning at 24H but not at 72H significantly altered lesion development. Vaginal viral replication was also significantly reduced with either 1% or 0.3% HPMPC initiated at 24H. In this study, HPMPC was more efficacious than 5% ACV. Since mice appear less susceptible to toxicity of HPMPC than guinea pigs, we then tested HPMPC in a genital HSV-2 infection of mice at 5%, 1% or 0.5% given three times daily, beginning 6 or 24H after virus inoculation. All concentrations of HPMPC tested reduced vaginal viral replication regardless of time of initiation of therapy. ACV at 5% also reduced vaginal viral replication, but not as effectively as HPMPC. These results indicate that topical therapy with 1%, 0.5%, or 0.3% HPMPC was more effective than 5% ACV in the treatment of genital HSV-2 infections of guinea pigs and mice and suggest that HPMPC should be considered for topical use in humans.