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Pathophysiology and Treatment of Clinically Resistant Cytomegalovirus Retinitis

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CMV retinitis was prospectively studied in 100 patients with AIDS in whom 11 developed clinically resistant retinitis (CRR), defined as new activity or progression despite at least 8 consequitive weeks of induction doses of either foscarnet or ganciclovir. Fundus photography, pharmacokinetics, CMV cultures and sensitivities, and survival analyses were studied. The therapeutic interventions attempted after CRR was identified included continuing high dose (induction level) of the same antiviral drug, changing the antiviral drug, and combination antiviral therapy with foscarnet and ganciclovir. CRR, occured in 11 of 100 (11%) of CMV retinitis patients and appeared to be a manifestation of acquired CMV antiviral drug resistance. Drug metabolism and pharmacokinetics in these patients were normal. The use of combination therapy with foscarnet and ganciclovir was effective in halting the progression of retinitis in 3 (75%) of 4 patients receiving combination therapy. CRR is a manifestation of infection by CMV which has acquired drug resistance. In these patients, combination antiviral drug treatment should be considered. It is likely that CRR will become more frequent as patients with CMV retinitis and AIDS survive longer.

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Long Acting Therapy of Viral Retinitis with HPMPC

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HPMPC, a high potency anti-herpes and anti-CMV drug was evaluated in the treatment of experimental retinitis caused by preretinal Herpes simplex injection in rabbits. HPMPC 100μg was intravitreally injected 10,15,21,30 or 46 days before, or 3,5 or 7 days after viral inoculation. Ganciclovir 200μg/0.1 ml was intravitreally injected 3,7 or 10 days prior to HSV-1 inoculation or 3,5 or 7 days after viral inoculation. Eyes pretreated with HPMPC were protected for 15 to 21 days. Ganciclovir did not protect completely even if administered at 3 days pre-inoculation. Treatment of established retinitis with HPMPC markedly inhibited the infection. HPMPC appears to have a remarkably potent and prolonged (up to one month) antiviral effect in our retinitis model and may prove more useful than ganciclovir in local treatment of CMV retinitis. Further studies were performed using liposome encapsulated HPMPC. The liposome system was designed to allow prolonged release of drug and was found to be non toxic to the eye. Liposome encapsulation enhanced the duration of the protective effect of HPMPC by a factor of four.