



THE OCULAR IMMUNOLOGY
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Experimental Murine Herpes Simplex Retinitis

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von Szily first observed a fascinating phenomenon in rabbits during his experiments on herpes simplex uveitis. He observed that, after injecting live herpes simplex virus into the right anterior chamber of a rabbit, not only an impressive anterior uveitis of the injected (right) eye developed, but, ten days later, a rapidly destructive retinitis of the opposite (left) eye developed. Histopathologic analysis of the inoculated eye disclosed that the retina of the injected (right) eye was completely spared of this destructive phenomenon.

The model was adapted to inbred mice in an effort to more thoroughly study the immunologic characteristics of this fascinating phenomenon. The same process develops in mice. That is, live HSV injection into the right anterior chamber results in anterior uveitis with, ten days later, contralateral necrotizing retinitis with ipsilateral retinal sparing. Live herpes virus is found in both the injected and in the uninjected eye, but it is not the virus itself which accounts for the retinal destruction, but rather the host's inflammatory response. T cells, macrophages, and natural killer cells are the cells primarily responsible for the destruction of the contralateral retina.

We have shown that it is the CD4 T cell and macrophages which are primarily responsible for the contralateral retinal destruction, and CD8 regulatory T cells provide some protection against this destruction. Similarly, natural killer cell depletion and macrophage depletion also confer some protection. We wondered whether or not oral acyclovir and/or HSV antibody therapy could also provide protection.

We therefore engaged in a study of the pharmacomanipulation of HSV-1 induced chorioretinitis in mice. Dr. Amyna Merchant was the primary investigator on the study. We discovered that contralateral chorioretinitis developed in none of the mice receiving acyclovir from post inoculation day 1, but did develop in 60% of the mice who had delay in institution of acyclovir therapy until in postinoculation Day 7. Contralateral retinitis developed in 50% of the mice receiving anti HSV antibody therapy from postinoculation Day 1, and in nearly 90% of mice with such treatment beginning at postinoculation Day 7.

These results, coupled with the clinical experience in treating patients with acute retinal necrosis, and coupled with our prior experience in acyclovir therapy for patients with recurrent HSV uveitis indicate that

treatment with acyclovir prominently reduces the incidence of contralateral herpes simplex virus-induced chorioretinitis in the von Szily model of herpes uveitis in mice, and lends support to the idea of systemic acyclovir for recurrent uveitis secondary to herpes.