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Human Cytomegalovirus (HCMV) Ocular Infection- A Rabbit Model of Chorioretinal Disease. EC Dunkel, ML Siegel, D Freitas, D Pavan-Langston, Eye Research Institute and Department of Ophthalmology, Harvard Medical School, Boston, MA, USA.

CMV ocular infection in immunocompromised individuals induces a progressive retinitis resulting in retinal necrosis, detachment and blindness. Currently available animal models of CMV infection have used non-human CMV strains that only approximate CMV disease states in humans. In this study, HCMV strain AD 169 was adapted by serial passage to rabbit corneal epithelial cells (SIRC). 10^5 to 10^6 PFU of adapted virus was used to inoculate immunocompetent NZW and pigmented rabbits (n=55). On days 2-4 PI, 85% of inoculated animals developed a mild vitritis that progressed rapidly and obscurred retinal observation by days 5-8 PI. Focal dense white areas of retinal necrosis were observed in all animals (days 3-6 PI); focal retinal microhemorhages similar to pathology in patients with HCMV retinitis were observed in all animals. HCMV disease resolved in 21 to 56 days. 45% of the HCMV inoculated animals developed a keratitis characterized by multiple, focal irregular annular white lesions in the anterior corneal stroma. HCMV was recovered by whole-cell and cell-free co-culture from iris, lens, vitreous, and chorioretinal tissues in the infected eyes. Pathological observation demonstrated multiple areas of white focal necrosis along the vascular arcades, and associated with the intraretinal hemorrhages. Histopathological analysis of chorioretinal tissues showed partial to complete loss of normal retinal lamellar architecture, focal retinal thinning with fibrocytic cells, a moderate to severe monocytic and polymorphonuclear leukocytic infiltrates in all retinal layers, scattered distended retinal megalic cells, intracytoplasmic HCMV inclusions and retinal detachment. Choroidal pathology showed vascular congestion and moderate to severe monocytic infiltrates; the iris was diffusely infiltrated with monocytic cells. This retinitis model can be used to evaluate anti-CMV therapeutic efficacy of compounds administered locally and systemically on Human CMV.

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An Animal Model of Neonatal Herpes Simplex Virus Infection. M.G. Myers, F.J. Bravo, D.I. Bernstein, B.L. Connelly, C.J. Harrison, L.R. Stanberry. Children's Hospital Research Foundation, Cincinnati, Ohio, U.S.A.

The pathophysiology and treatment of perinatal HSV infections are incompletely defined because of the lack of a suitable animal model that is analogous to infection of the newborn human. We report here the natural history of neonatal HSV infection in guinea pigs, which may represent such a model. Newborn outbred Hartley animals were inoculated intranasally with HSV-2 MS strain (5.9 $\log_{10}$ pfu in 30 ul) within 24 hours of birth. Three to 7 days later, 32 of 33 animals developed vesicular rash on the mucosa of the nose, mouth, eyelids and skin of the snout. Between days 6-9, 75% exhibited respiratory disease. Half the animals died before day 10, but none afterwards. Virus was recovered from brain (3.0 $\log_{10}$ pfu/g), liver (3.3), lung (3.5), brain stem, trigeminal ganglia and adrenal glands from animals that died or were moribund. However, during the first several days after infection, virus was recovered from the central nervous system (CNS) but not other sites, including the blood. Surviving animals recovered between days 8 to 17, but developed clinically apparent recurrent lesions on the nose, mouth and eyelids over a 30-day period. In summary, HSV-2 infection of the newborn guinea pig results in rapid spread of virus to the CNS and then multi-organ disease with high, but not universal, mortality. This model should be useful for the studying of the pathophysiology of neonatal HSV, developing new strategies for the control of neonatal herpes, and evaluating putative antiviral drugs.