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In Vitro and In Vivo Characterization of Herpes Simplex Virus Isolates Recovered from HIV+ Patients. E. L. Hill, G.A. Hunter, and M. N. Ellis. Burroughs Wellcome Co., Res. Tri. Park, N.C., USA.

In patients with normal immunity ACV resistance has not been a significant clinical problem. However, in the immunocompromised patient ACV-resistant HSV can cause locally progressive disease. Concern that isolates shed by HIV+ patients might possess novel mechanisms of resistance or be more virulent than previously reported resistant isolates led us to evaluate these isolates in vitro and in vivo. In vitro analysis of the clinical isolates was by the dye uptake assay, differential plaque autoradiography, and enzyme kinetics. Of the 100 isolates recovered from 51 patients, 77 were ACV resistant with ED_{50} values of >3 ug/ml. Of these 77 resistant viruses, 75 had a thymidine kinase-deficient (TKd) phenotype and 2 had a TK-altered (TKa) phenotype. All ACV-sensitive isolates possessed a wild type TK. The cutaneous virulence of selected isolates was determined in hairless (HRS/J) and athymic mice, while neurovirulence was determined in BALB/C mice. Our results indicate that HSV isolates recovered from HIV+ patients are similar in drug susceptibility and animal pathogenicity to HSV isolates recovered from normal patients and non-AIDS immunocompromised patients. At the present time, it is difficult to determine the incidence of resistance in this population because only isolates from treatment failures are sent to us for analysis.

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Sequence Analysis of the Thymidine Kinase Genes of Acyclovir-Resistant Varicella Zoster Virus Isolates. C. Talarico, W. Phelps, K. Biron. Burroughs Wellcome Co., Research Triangle Park, NC, USA

AIDS patients often experience recurrent infections with varicella zoster virus (VZV) which require repeated or prolonged treatment with acyclovir. We have documented *in vitro* resistance of isolates recovered from four patients after treatment failure (Jacobson, *et al.* Annals of Internal Med. 112:187-191, 1990.). Sequence analysis of PCR-amplified DNA encoding the thymidine kinase (TK) of plaque-purified virus from these clinical isolates showed sequence changes. Viral strains isolated from two patients had nucleotide deletions in the TK DNA. These deletions introduced a premature termination codon which is expected to result in the production of a truncated protein. Immunoprecipitation of extracts from cells infected with these virus strains showed no detectable TK. Viral strains from the other two patients had nucleotide substitutions located in the proposed nucleoside-binding site of the TK protein which may be expected to change the substrate specificity of the TK. Immunoprecipitation of extracts from cells infected with these virus strains suggested that a full length TK protein was synthesized. Susceptibililities of these virus strains to TK dependent, candidate anti-VZV agents in the 5-substituted uracil arabinoside class were determined.