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### ATYPICAL MANIFESTATIONS AND POOR OUTCOME OF HERPES SIMPLEX ENCEPHALITIS IN THE IMMUNOCOMPROMISED

**Richard B. Tenser, Hershey, PA:** In the article by Tan et al.,<sup>1</sup> atypical illness and poor outcome of HSV encephalitis in immunocompromised patients was likely due to their immune status, and possibly also to antiviral-resistant mutant HSV. Acyclovir and related antivirals are phosphorylated by the HSV-encoded thymidine kinase (TK) to the active antiviral state.

However, during HSV infections, mutants arise that are acyclovir resistant primarily because they lack viral TK activity (TK<sup>-</sup>) and do not phosphorylate acyclovir.<sup>2</sup> In non-immunosuppressed HSV-infected individuals treated with acyclovir, wild-type TK + HSV is inhibited by acyclovir, and the small amounts of TK<sup>-</sup> HSV that develop are likely controlled by the

immune system. However, in immunocompromised individuals, while wild-type TK + HSV is inhibited by acyclovir, TK<sup>-</sup> mutants likely multiply.

We used an isotope plaque assay to estimate proportions of TK<sup>-</sup> and TK<sup>+</sup> HSV in lesion swabs from an immunocompromised patient treated with acyclovir.<sup>3</sup> TK<sup>-</sup> HSV does not replicate well in non-dividing cells but does in replicating cells. In immunocompromised patients,<sup>1</sup> it is suggested that during the period of acyclovir treatment, TK<sup>-</sup> HSV probably replicated, more likely in glial cells than in neurons. Presumptive TK<sup>-</sup> HSV may have contributed to the atypical clinical course of these patients.

**Author Response: Avindra Nath, Bethesda, MD:** I thank Dr. Tenser for his comments and for agreeing that acyclovir-resistant HSV may have played a role in the pathophysiology of encephalitis in these patients.

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## Atypical manifestations and poor outcome of herpes simplex encephalitis in the immunocompromised

Richard B. Tenser and Avindra Nath

*Neurology* 2013;81;514

DOI 10.1212/01.wnl.0000433164.29848.92

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