3. Tomlinson SE, Bostock H, Grinton B, et al. In vivo loss of slow potassium channel activity in individuals with benign familial neonatal epilepsy in remission. *Brain* 2012;135: 3144–3152.
4. Tomlinson S, Burke D, Hanna M, Koltzenburg M, Bostock H. In vivo assessment of HCN channel current (I_h) in human motor axons. *Muscle Nerve* 2010;41:247–256.
5. Howells J, Trevillion L, Bostock H, Burke D. The voltage dependence of I_h in human myelinated axons. *J Physiol* 2012;590:1625–1640.

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

Richard B. Tenser, Hershey, PA: In the article by Tan et al.,¹ 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[−]) and do not phosphorylate acyclovir.² In non-immunosuppressed HSV-infected individuals treated with acyclovir, wild-type TK + HSV is inhibited by acyclovir, and the small amounts of TK[−] HSV that develop are likely controlled by the

immune system. However, in immunocompromised individuals, while wild-type TK + HSV is inhibited by acyclovir, TK[−] mutants likely multiply.

We used an isotope plaque assay to estimate proportions of TK[−] and TK⁺ HSV in lesion swabs from an immunocompromised patient treated with acyclovir.³ TK[−] HSV does not replicate well in non-dividing cells but does in replicating cells. In immunocompromised patients,¹ it is suggested that during the period of acyclovir treatment, TK[−] HSV probably replicated, more likely in glial cells than in neurons. Presumptive TK[−] 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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1. Tan IL, McArthur JC, Venkatesan A, Nash A. Atypical manifestations and poor outcome of herpes simplex encephalitis in the immunocompromised. *Neurology* 2012;79:2125–2132.
2. Sarisky RT, Quail MR, Clark PE, et al. Characterization of herpes simplex viruses selected in culture for resistance to penciclovir or acyclovir. *J Virol* 2001;75:1761–1769.
3. Westheim AI, Tenser RT, Marks JG. Acyclovir resistance in a patient with chronic mucocutaneous herpes simplex infection. *J Am Acad Dermatol* 1987;17:875–880.

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Richard B. Tenser and Avindra Nath

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