

**Familial Herpes Simplex Encephalitis**

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Herpes simplex encephalitis (HSE) is a sporadic encephalitis with an incidence of about 2 to 4 cases per million population per year.<sup>1,2</sup> The occurrence of HSE in two members of a family has only rarely been reported.<sup>3,4</sup> We have identified HSE in a mother and her son within an interval of over 21 years.

A 14-year-old boy developed an illness in July 1979 with fever, headache, nausea, confusion, and partial seizures. An initial computed tomography head scan was normal and an electroencephalogram showed intermittent theta and polymorphous delta activity with predominance over the right hemisphere. Cerebrospinal fluid analysis showed 241 white blood cells (95% lymphocytes and 5% polymorphonuclear leukocytes) and 10 red blood cells/ $\mu$ L; cerebrospinal fluid protein was 70mg/dL and glucose 90mg/dL. Therapy was initiated with intravenous adenosine arabinoside. He developed status epilepticus within 72 hours of admission. Electroencephalograms showed epileptiform activity over the left temporal region that extended widely across the left hemisphere and, later, sporadic epileptiform activity was also noted from the right hemisphere. A repeat computed tomography head scan showed hypodense lesions in the left frontal and temporal lobes with mass effect and contrast enhancement. He died after a 2-week hospital course. Post-mortem examination showed hemorrhagic necrosis bilaterally in the temporal lobes. Microscopy revealed leptomeningeal and perivascular inflammatory cell infiltrates and scattered neuronal intranuclear inclusions. Immunohistochemistry demonstrated strong labeling for herpes simplex virus 1 antigen in multiple neurons (Fig A) and glial cells; ultrastructural studies showed virions about 100nm in diameter consistent with herpes simplex virus.

In November 2000, his mother at age 68 developed an illness with headache, mild aphasia, confusion, and mild fever. She had a generalized seizure after admission to hospital and an electroencephalogram showed irregularly repetitive sharp wave and focal delta activity in the left temporal region. A magnetic resonance imaging scan showed lesions in the left medial temporal lobe and the insular cortex on T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences (see Fig B). Cerebrospinal fluid showed 173 white blood cells (100% mononuclear cells) and 326 red blood cells/per  $\mu$ L; cerebrospinal fluid protein was 97mg/dL and glucose 74mg/dL. Herpes simplex virus 1 DNA was detected in the cerebrospinal fluid with polymerase chain reaction amplification. She was treated with a 21-day course of intravenous acyclovir and showed clinical improvement. She had mild residual impairment of memory and mild aphasia, and she was able to continue to live independently.

Familial HSE has been the subject of two previous reports. The first described HSE in 2 sisters with an interval of

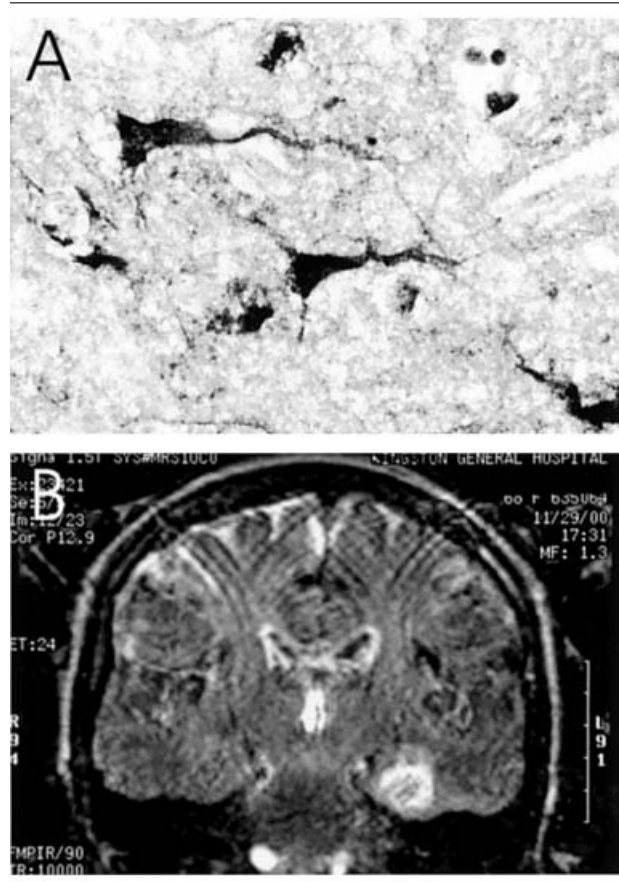


Fig. (A) Temporal lobe cortex from autopsy of 14-year-old boy showing immunoperoxidase staining for herpes simplex virus 1 antigen in neurons and neuronal processes. (B) Magnetic resonance imaging during his mother's illness showing hyperintense signal in the left medial temporal lobe on fluid-attenuated inversion recovery (FLAIR) sequences. (A) Magnification  $\times 430$ .

8 years;<sup>3</sup> the second described HSE in 2 brothers within a 13-year interval.<sup>4</sup> We now report fatal HSE in a 14-year-old boy followed by HSE affecting his mother over 21 years later, and we believe that this is the first report of HSE in both a parent and child. In combination with the two previous reports of familial HSE, this suggests the possibility of an increased genetic susceptibility to the occurrence of HSE in these cases. Alternatively, strains of herpes simplex virus with enhanced neuroinvasive or neurovirulent properties<sup>5</sup> may be transmitted between family members or they may share a common source, and these strains may be more likely to cause HSE upon reactivation years later. These familial cases raise suspicion that there are biologic factors involving the host, the virus, or both, that favor familial occurrence of HSE and that familial cases are not merely random occurrences.

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## Effective Treatment for Essential Tremor

Robert R. Young, MD

The study by Louis and colleagues<sup>1</sup> of the prevalence of essential tremor (ET) is certainly important and represents an enormous amount of work. Their statement that ET is a disorder that “is chronic, often progressive, and disabling and for which there are few effective therapies” is clearly true but is more pessimistic than need be. At least one therapy for ET is extremely effective, namely deep brain stimulation (DBS) of the thalamus,<sup>2–4</sup> particularly nucleus VPLa,<sup>5</sup> and is very safe.<sup>5</sup>

Although ET may be 20 times more prevalent than Parkinson’s disease, the numbers of patients with ET seen in Movement Disorders Clinics are much fewer than those figures would suggest. The number of those seriously impaired by their tremor who reach a Deep Brain Stimulation Clinic for consideration of surgery for their disability is much smaller yet, certainly less than one-third of those sent for evaluation for surgery for Parkinson’s disease.

I suspect our failure to see most of those whose tremor we could alleviate is attributable to the concept, held by patients, their families, and their physicians, that “there are few effective therapies” and, as their relatives have done, patients must learn to live with the tremor. An antisurgical pessimism obviously exists among neurologists, particularly older ones, but I hope it can be overcome now that DBS, in the right hands, has been shown to afford excellent relief of tremor. As Louis and colleagues demonstrate, at least 20% of the increasing elderly population will develop ET. If they are not aware of the benefits of DBS, a large percentage of the elderly will be needlessly handicapped by their tremor. We need to educate our colleagues as well as family physicians and the population at large. Most persons of any age need not be handicapped by ET.

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## Reply

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Young makes the important point that deep brain stimulation is an effective treatment for essential tremor (ET) and, as noted in our article<sup>1</sup> and elsewhere,<sup>2</sup> deep brain stimulation can provide relief for severe medically intractable cases. We have found, however, that one of the major obstacles is patient reluctance to undergo brain surgery and have a mechanical device implanted under their skin. Young also alludes to the fact that the proportion of community-dwelling ET cases who seek medical attention is small,<sup>3</sup> although most have some functional disability.<sup>4</sup> Several potential explanations have been proposed. First, the tremor is often viewed as a constitutional idiosyncrasy or an unavoidable consequence of the normal aging process, rather than the result of a potentially treatable disease that has a cause, a well-defined natural history, and an (albeit unknown) underlying pathophysiology. Second, although it may be functionally disabling, the disease is regarded as “benign” because it is not thought to be associated with an increased risk of adverse outcomes, such as morbidity or mortality. However, few data are available, and this requires further study. Finally, some people may be reluctant to seek medical attention because of the slow evolution of symptoms, allowing them to make necessary-adjustments and modifications. As Young points out, many people with ET choose to “learn to live with the tremor” rather than seek medical or surgical treatment.

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