involving Centers in Australia, UK, and Canada. (Wallace RH, Scheffer IE et al. Neurology 2003;61:765-769). A family history of seizures was noted in 17 (68%) of SMEI patients.

PATHOPHYSIOLOGY OF SEIZURES WITH BRAIN TUMORS

The etiology of tumor-related seizures (TRS) is reviewed from the Karolinska Institute, Stockholm, Sweden, and University of Pennsylvania, Philadelphia. Multiple causes are considered, involving host and tumor factors. Morphological changes (aberrant neuronal migration, alterations in glial gap-junction coupling), alkaline peritumoral pH, and ion level and amino acid changes (abnormal glutaminergic transmission) in peritumoral brain tissue are probable factors in TRS pathophysiology. Several alterations in enzymatic pathways (eg. lactate dehydrogenase, glutamine synthetase) are observed in epileptic and neoplastic tissues. Cytokines, and tumor necrosis factor in particular, have neuromodulatory effects, and are rapidly induced in glial cells following seizures.

The efficacy of antiepileptic drugs (AED) in TRS is poor, and prophylactic use of AEDs in TRS is not generally recommended. TRS mechanisms (morphological changes, altered receptor patterns, and induction of cytokines) are not influenced by most AEDs. An antineoplastic effect of valproic acid (VPA) is under investigation. Overcoming drug-resistance protein activity (glycoprotein P) may improve response of TRS to AEDs. (Schaller B, Ruegg SJ. Brain tumor and seizures: pathophysiology and its implications for treatment revisited. Epilepsia 2003;44:1223-1232). (Reprints: Dr B Schaller, Department of Neuroscience, Karolinska Institute, Retzius vag 8, S-17177 Stockholm, Sweden).

COMMENT. The records of 291 consecutive children treated for intracranial tumor at the Mayo Clinic from 1950-1959 were analyzed with particular attention to those with seizures (Backus RE, Millichap JG. Pediatrics 1962:29:978-984). Seizures occurred in 17% of the total group – in 25% of patients with supratentorial tumors and in 12% of those with infratentorial tumors. Seizures were the initial symptom in 15% with supratentorial and 1% with infratentorial tumors. Average age at onset of tumor-related seizures was 4.9 years. Diagnosis of supratentorial tumors was delayed for an average of 2 years after the initial seizure, whereas infratentorial tumors were diagnosed within 3 months of the seizure onset. Seizures were more common with slowly growing astrocytomas (67% incidence) than with grades 3 and 4 gliomas (10%). Increased intracranial pressure was present with the first seizure in 79% of infratentorial tumors compared to only 20% of supratentorial tumors.

In a study of 560 patients with supratentorial brain tumor at Walton Hospital, Liverpool, UK, a seizure was the first symptom in 164 (30%). (Smith DF et al. J Neurol Neurosurg and Psychiatry 1991;54:915-920). Patients presenting with epilepsy were diagnosed late (mean, 28 months cf 4 months with other symptoms) but had a longer survival (37 months) than those with other symptoms (6 months survival). They were more likely to have a normal neurologic exam and a low-grade tumor. Increasing age at tumor diagnosis, focal neurologic signs, an enhancing CT lesion, surgical biopsy, and male sex were significant independent variables adversely affecting prognosis. Primary IC tumors presenting with epilepsy were relatively benign. They were less likely to receive radiotherapy or biopsy, but more likely to undergo resective surgery. Early resective

surgery or radiotherapy were of no benefit. Seizures were refractory to AEDs, only 11 of 164 patients achieving a 1 year remission. The control of tumor-related epilepsy poses a special problem, requiring more specific AEDs. (See Progress in Pediatric Neurology II, PNB Publ, 1994;pp344-345).

Progressive myoclonus in a 22-month-old boy with a deep cerebellar ganglioglioma is reported from the University of Rochester, NY (Mink JW et al. Neurology 2003;61:829-831). The authors theorize that myoclonus resulted from abnormal paroxysmal output from cerebellar nuclei, and was not a case of "cerebellar epilepsy."

The impact of epilepsy and AED treatment on cognitive functioning was studied in 156 patients with low-grade gliomas. (Klein M et al. Ann Neurol 2003;54:514-520). Of 86% with epilepsy, 50% of those on AEDs were seizure-free. Compared to healthy controls, glioma patients had significant reductions in psychomotor function, attention, memory, and quality of life. Cognitive dysfunction was attributed to adverse effects of AEDs, whereas decline in quality of life was ascribed to incomplete seizure control.

CHRONIC EPILEPSY AND COGNITION

Cognition, change of memory and nonmemory functions, in 147 surgically and 102 medically treated patients with temporal lobe epilepsy was evaluated in a longitudinal study at the University of Bonn, Germany, and the University of Sheffield, UK. Patients were tested at baseline (T1) and after 2 to 10 years (T3). Surgical patients were also retested 1 year postoperatively (T2). Higher baseline test performance was predictive of better long-term performance and better cognitive outcome. Complete seizure control was obtained in 63% of surgical and 12% of medically treated patients. Significant decline in memory (with little change in nonmemory) function had occurred at T3 follow-up in 50% of medical and 60% of surgical patients. More limited surgical resections were associated with better cognitive outcome and less risk of cognitive decline. Seizure-free surgical patients showed recovery of nonmemory at T2 ($p<0.001$), and of memory functions at T3 ($p=0.03$). Psychosocial outcome was better when seizures were controlled. (Helmstaedter C, Kurthen M, Lux S, Reuber M, Elger CE. Chronic epilepsy and cognition: a longitudinal study in temporal lobe epilepsy. Ann Neurol October 2003;54:425-432). (Respond: Dr Helmstaedter, University of Bonn, Department of Epileptology, Sigmund Freud Strasse 25, 53105 Bonn, Germany).

COMMENT. Both surgically and medically teated patients with temporal lobe epilepsy (TLE) are at risk of cognitive decline. The degree of cognitive decline is inversely related to seizure control. Surgically treated compared to medically treated patients have better seizure control. When unsuccessful, however, surgery may accelerate the cognitive decline seen with failed medical treatment, especially with left sided temporal lobe resections. When seizures are controlled, either medically or surgically, memory decline is halted or even reversed. Nonmemory functions, related to brain regions distant from the focus, recover more quickly than memory deficits directly associated with the focus. Early and complete control of seizures is necessary to prevent cognitive impairment and adverse effects on quality of life and learning. Memory outcome and that of school or work performance are interrelated, emphasizing the importance of early seizure control. (See Editorial. Duncan JS, Thompson PJ. Ann Neurol 2003;54:421-422).