IS EPILEPSY A PROGRESSIVE DISEASE?

E. Beghi
Laboratory of Neurological Disorders, Istituto Mario Negri, Milano, Italy

Studies published in the first half of the last century invariably showed that the percentage of patients achieving prolonged or permanent seizure remission does not exceed 30% (Rodin, 1968). These data supported the opinion that epilepsy is a persisting clinical condition in the vast majority of the patients. This belief, based on the results of observations done in patients seen in tertiary health care facilities, was contrasted by the results of more recent studies in representative cohorts of newly diagnosed patients followed prospectively after treatment start. These studies led to two major conclusions: 1. the percentage of patients achieving remission after treatment start is much higher than previously indicated (up to 70-80% of cases) (Annegers et al, 1979; Cockerell et al, 1997); 2. The earlier the treatment the higher the remission rate. This latter observation supported the idea that epilepsy is a progressive disease and that treatment should be started as soon as possible after treatment start, ideally after the first seizure. However, several subsequent observational and experimental studies provided evidence against this idea. First of all, a number of studies done in developing countries showed that remission rates can be fairly high even in undertreated or untreated patients (Watts, 1992; Placencia et al, 1994; Wang et al, 2006). Second, studies comparing early and late treatment of epilepsy failed to document differences in the remission rates (Feksi et al, 1991). Third, two large randomized clinical trials consistently showed that treatment of the first seizure may be followed by a lower risk of relapse in the first two years but does not affect the long-term prognosis of epilepsy (i.e., the chance of 1, 2, and 5-year remission of seizures) (Musicco et al, 1997; Marson et al, 2005). Fourth, treatment of patients with acute symptomatic seizures caused by differing CNS injuries does not prevent the occurrence of unprovoked seizures and epilepsy (Temkin, 2001).
Other *observations seem to support the idea that epilepsy is <u>not</u> a progressive disease: 1. several seizure patterns have been identified and none seems to detect a progressive course of the disease in a patient with idiopathic or cryptogenic epilepsy (Shorvon & Luciano, 2007; Sillampaa & Schmidt, 2007); 2. The incidence of subsequent epilepsy is not increased after cryptogenic convulsive status epilepticus in children (Raspall-Chaure et al, 2006).*

We agree with Warren Blume (2006) that "[p]rognosis for seizure control and cognitive development varies considerably among [epilepsy] syndromes. Several factors may interact to influence outcome of epilepsy including causative etiology, ictal and interictal discharges, seizure-related trauma or systemic perturbations, and antiepileptic drug (AED) effects. Clinical evidence convincingly supporting Gowers' hypothesis that seizures beget seizures is lacking. Short-term seizure suppression by early treatment does not appear to influence long-term prognosis. Malignant epilepsy syndromes usually begin in infancy or childhood, have a high seizure frequency, resist the initial AED, and are often associated with progressive cognitive dysfunction. However, prompt management of some severe epilepsy syndromes may lessen cognitive decline… Several experimental paradigms closely parallel human [temporal lobe epilepsy] (TLE) as both have an initial precipitating injury (IPI), a latent period, then recurrent spontaneous seizures. In humans, an IPI is any medical event with neurological implications. Although transition from a latent period to a seizure disorder certainly constitutes "progression" of the disorder, convincing clinical evidence of subsequent worsening has not emerged. Substantial clinical and experimental evidence indicates some cognitive regression and focal atrophy with time for TLE and other intractable syndromes. However, seizure frequency and severity, established early in the disorder, appear stable in most patients, and even regress in benign syndromes."

References

Annegers JF, Hauser WA, Elveback LR. Remission of seizures and relapse in patients with epilepsy. Epilepsia 1979; 20: 729-737.
Blume WT. The progression of epilepsy. Epilepsia 2006; 47 (suppl 1): 71-78.
Cockerell OC, Johnson AL, Sander JWAS, et al. Prognosis of epilepsy: a review and further analysis of the first nine years of the British National General Practice Study of Epilepsy, a prospective population-based study. Epilepsia 1997; 38: 31-46.
Feksi AT, Kaamugisha J, Sander JWAS. Comprehensive primary health care antiepileptic drug treatment programme in rural and semi-urban Kenya. Lancet 1991; 337: 406-409.
Marson A, Jacoby A, Johnson A, et al. Immediate versus deferred antiepileptic drug treatment for early epilepsy and single seizures: a randomised controlled trial. Lancet 2005; 365: 2007-2013.
Musicco M, Beghi E, Solari A, et al. Treatment of first tonic-clonic seizure does not improve the prognosis of epilepsy. Neurology 1997; 49: 991-998.
Placencia M, Sander JW, Roman M, et al. The characteristics of epilepsy in a largely untreated population in rural Ecuador. J Neurol Neurosurg Psychiatry 1994; 57:320-325.
Raspall-Chaure M, Chin RF, Neville BG, Scott RC. Outcome of pediatric status epilepticus: a systematic review. Lancet Neurol 2006; 5: 769-779.
Rodin EA. The prognosis of patients with epilepsy. Springfield, IL, Charles C Thomas, 1968.
Shorvon SD, Luciano AL. Prognosis of chronic and newly diagnosed epilepsy: revisiting temporal aspects. Curr Opin Neurol 2007; 20: 208-212.
Sillanpaa M, Schmidt D. Natural history of treated childhood-onset epilepsy: prospective, long-term population-based study. Brain 2006; 129: 617-624.
Temkin NR. Antiepileptogenesis and seizure prevention trials with antiepileptic drugs: meta-analysis of controlled trials. Epilepsia 2001; 42: 515-524.
Wang WZ, Wu JZ, Ma GY, et al. Efficacy assessment of phenobarbital in epilepsy: a large community-based intervention trial in rural China. Lancet Neurol 2006; 5: 46-52.
Watts AE. The natural history of untreated epilepsy in a rural community in Africa. Epilepsia 1992; 33: 464-468.