

## INTRACTABLE EPILEPSY: DEFINITION AND NEUROBIOLOGY

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Approximately 20% of individuals with a diagnosis of epilepsy have seizures that are not adequately controlled by antiepileptic drugs. In some of these, the patients fail to respond because their paroxysmal events are not epileptic; in others, an incorrect treatment plan has been prescribed, either due to misdiagnosis of seizure type or misinformation about appropriate therapy; and in still others, patients are noncompliant and do not take their medications properly. There are, however, a significant group of patients with medically uncontrolled seizures that do not respond to appropriate antiepileptic drug management, and these have been referred to as "medically intractable." Many types of epilepsy can be refractory to pharmacotherapy, but these are usually symptomatic disorders, including certain catastrophic epilepsies of infancy and early childhood, the Lennox-Gastaut syndrome, and a variety of localization-related epilepsies. Because virtually all antiepileptic drugs reach the market after screening against animal models of generalized convulsive and absence seizures, it is not surprising that they are ineffective against epileptic disorders associated with ictal events that represent different pathophysiological mechanisms, such as drop attacks and complex partial seizures of limbic origin. A recent study from a major epilepsy center indicated that 25 to 50% of their patients had mesial temporal lobe epilepsy (MTLE), that form of temporal lobe epilepsy associated with hippocampal sclerosis, and that these patients were the most refractory to medical treatment. MTLE, therefore, may be the most common form of intractable epilepsy. The fundamental mechanisms of seizure generation in this disorder appear to be different from those in neocortical or primary generalized epilepsies, indicating the need for instituting new approaches to pharmacotherapy. In addition, approximately 80% of these patients can expect to become seizure free following anteromesial temporal lobectomy, and several other so-called intractable epilepsies can also be effectively treated with surgery. In all instances, early surgical intervention provides the best chance of a return to a normal lifestyle. In view of the fact that there are so many available antiepileptic drugs today that it would take a lifetime to try every one alone and in combination in a given patient, proving that a patient is truly medically intractable becomes impossible. The concept of intractable epilepsy, therefore, has become outmoded. When surgical treatment is a consideration, the new concept of surgically remediable syndromes would seem to be much more conducive to timely intervention.