Introduction

Alcohol abuse is one of the most common causes of adult-onset seizures. Earnest and Yarnell reviewed 472 adults who were admitted with seizures and found that 41% were related to alcohol abuse (1). A variety of etiologies for seizures related to alcohol exist, the most frequent being the partial or absolute withdrawal of alcohol following a period of heavy use. In addition, seizures may be caused by acute head trauma or alcohol-related toxic-metabolic disorders. Other factors noted to precipitate seizures in the setting of acute and chronic alcohol abuse include pre-existing idiopathic or post-traumatic epilepsy. The term alcohol-related seizures (ARSs) has been adopted in recognition of the multifactorial origin of seizures in the setting of acute and chronic alcoholism (2). Today the management of patients presenting with ARSs remains challenging, despite years of experience, observation, and study.

Historical Perspective

The observation that seizures occur as part of alcohol withdrawal was noted by Hippocrates around 400 B.C. (3). As early as 1852, Huss described the relationship of seizures to the withdrawal of alcohol, often described as “rum fits” (4). Victor and Adams first published clinical data in 1953 describing seizures as part of the withdrawal syndrome (5).

In a classic experimental study, Isbell and colleagues (6) observed 10 former heroin and morphine addicts abruptly withdraw from large doses of alcohol consumed over an extended period of time. Four subjects withdrew during
the course of the study. The remaining 6 subjects, who consumed alcohol for 48 d or more, all experienced symptoms of withdrawal, including tremor, vomiting, diarrhea, fever, and increased blood pressure. Seizures occurred in two subjects, and two others developed delirium tremens.

Subsequently Victor and Brausch studied 241 patients with a history of drinking alcohol and experiencing seizures (7). Despite such broad entrance criteria, a clinical syndrome emerged that included 90% of the patients.

The seizures, which occurred in approx. 10% of patients after the cessation of drinking, started in adulthood, following many years of heavy drinking. The seizures were noted to be generalized, tonic-clonic in type, often multiple (60%), and usually occurred 7–48 h after cessation of drinking. The interval from the first to the last seizure was 6 h or less in 85% of patients. The electroencephalograms (EEGs) were also found to be normal. A small group (7/241) had idiopathic epilepsy, and a clearly defined group (21/241) comprised patients with head trauma and alcohol dependence. The post-traumatic group frequently had focal seizures with focal EEG abnormalities. In patients with idiopathic and post-traumatic epilepsy, seizures occurred during periods of drinking but were far more frequent during periods of abstinence. The period of drinking required to precipitate seizures in both groups was brief; in some cases seizures occurred after a single evening of drinking.

**Pathogenesis of Seizures Related to Alcohol**

The biochemical mechanisms responsible for alcohol intoxication are complex, and no specific pathophysiologic mechanism completely explains all ARSs. Alcohol is known to be a general anesthetic with anticonvulsant properties (8). Alcohol administration causes alterations in membrane receptors that may be important in the pathogenesis of seizures. Alcohol specifically potentiates the postsynaptic effect of γ-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the brain (9). When the blood alcohol concentration is reduced, the habituated nervous system becomes hyperexcitable and produces symptoms of tremors, seizures, and delirium. Benzodiazepines may crossreact with alcohol, substitute for the withdrawal of the GABA-enhancing effect of alcohol, and diminish the signs and symptoms of withdrawal. Modulation of G proteins (10) and calcium channels (11) are other mechanisms by which seizures can be induced in alcoholics.

**Differential Diagnosis of Seizures in the Alcohol-Dependent Patient (Table 1)**

Multiple possible etiologies have been postulated regarding the association between alcohol and seizure activity.