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UPDATE ON EPILEPSY

Elson L. So, MD

Several major developments changed the clinical management of epileptic disorders in the past decade. These developments largely resulted from rigorous prospective and controlled clinical studies that began in the 1980s. These studies supported the formulation of scientific approaches to many long-standing clinical dilemmas that practitioners encounter in the management of seizure disorders. This article reviews some of the major advances in the care of patients with epilepsy.

THE FIRST SEIZURE: TO TREAT OR NOT TO TREAT

The objective of long-term antiepileptic drug (AED) therapy is to prevent the recurrence of seizures. Hence, chronic use of AED therapy is unnecessary when seizures are provoked by factors that can be identified and remedied. Such a clinical situation often occurs when seizures are acutely provoked by physical injuries, vascular insults, or metabolic or toxic disturbances (provoked seizures or acute symptomatic seizures). Correcting the provoking factors usually obviates AED therapy, whereas persistence of the factors may necessitate AED therapy. The dilemma of whether to initiate AED treatment arises when first seizures occur without provoking factors (unprovoked seizures). The decision would not be difficult if AED treatment was devoid of potential medical, social, or financial implications. However, in one study,[29] up to 23% of patients treated with AEDs had to be given another drug solely because of side effects. In another study,[19] as many as 8.5% of patients had to stop taking medications because of a rash. The use of AEDs sometimes complicates issues of employment qualification and insurance eligibility. Medical expense is increased because of the cost for the drug, blood level determinations, and follow-up visits with physicians. Moreover, there is still no proof that AED treatment reduces the risk of seizures after a first unprovoked seizure.[28] For these reasons, the use of an AED after a first unprovoked seizure is appropriate

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only when the expected benefits of taking the AED outweigh the potential risks and disadvantages.

This selective approach is supported by recent identification of factors that are predictive of seizure recurrence. In a prospective study involving primarily adults, the overall risk of recurrence after a first unprovoked seizure was 14% at 1 year, 29% at 3 years, and 34% at 5 years.[15] Patients with previous neurologic insults were more likely to have recurrent seizures than those without (idiopathic cases). Among those with neurologic insults, the risk of recurrence was increased by status epilepticus, the presence of Todd's paralysis, and the occurrence of provoked seizures in the past. Among the idiopathic cases, factors that increased risk were a spike-and-wave electroencephalographic (EEG) abnormality, the occurrence of provoked seizures in the past, and a history of epilepsy in a sibling. Although patients with idiopathic causes and no risk factors had the best prognosis, 23% still had recurrence at 5 years after the initial seizure. Patients with the worst prognosis—80% recurrence at 5 years—were those with neurologic insults and provoked seizures in the past.

In comparison with the foregoing study, a retrospective population-based study reported a higher overall recurrence rate—56% by 5 years.[3] Again, prognosis was more favorable if there was no previous neurologic insult. Among the idiopathic cases, factors associated with higher recurrence rates were focal seizure type, EEG abnormalities, and abnormal findings on neurologic examination. Among patients with previous neurologic insults, focal seizure type was the only poor prognostic factor.

A prospective study of children revealed that the overall risk of recurrence was 26% at 1 year, 40% at 2 years, and 42% at 4 years after a first unprovoked seizure.[34] Among those with previous neurologic insults, the risk of recurrence was increased when the first unprovoked seizure was a focal seizure or when a febrile seizure had occurred in the past. Among children whose first seizures were idiopathic, the risk of recurrence was increased by the presence of EEG abnormalities. A history of epilepsy in first-degree relatives was also a risk factor, but only in children with abnormal EEG results. Children whose first seizures were idiopathic and who had normal EEG results had the best prognosis. Their risk of recurrence was 23% at 2 years. However, the risk at 2 years increased to 50% when EEG results were abnormal. Similar to the pattern in adults, the next seizure tended to occur within 1 year after the first unprovoked seizure.

The decision regarding AED treatment should not be based solely on the probability of seizure recurrence. The clinician and the patient should also assess the potential social, occupational, and psychologic consequences of experiencing more seizures. For example, an adult who drives for a living may elect to have AED treatment because his or her first seizure was a generalized tonic-clonic seizure that occurred without warning. Alternatively, the Committee on Drugs of the American Academy of Pediatrics does not recommend treatment for most children after a first unprovoked seizure.[1] Also, initial seizures that herald some benign epilepsy syndromes in childhood may not require therapy because recurrent seizures in these syndromes may not be disabling and the probability of spontaneous remission may be good (such as in benign rolandic epilepsy). After careful counseling and guidance by the clinician, the decision ultimately belongs to the patient and to the guardian.

Certain types of seizures are by nature recurrent (for example, absence seizures and myoclonic seizures). The foregoing studies specifically excluded these types of seizures. The clinician should make certain that the seizure under consideration was indeed the only unprovoked seizure ever experienced.

Careful interview may sometimes disc
patients presenting with generalized
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OPTIMIZING SINGLE-DRUG THERAI

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Several AEDs are available for the
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Table 1. STEPS TO FOLLOW WHEN CON
TREATMENT AFTER A FIRST SEIZURE

	First
Provoked	
Consider whether provoking factor can be corrected	Estimate re Assess cor
If yes, AED treatment is unnecessary	recurrenc social, oc
If no, AED treatment should be considered	psycholo Consider p prefere Consider w outwei
	If yes, ac treatm
	If no, witl treatm

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by recent identification of factors that prospective study involving primarily r a first unprovoked seizure was 14% rs.[15] Patients with previous neurologic nt seizures than those without (idio- gic insults, the risk of recurrence was esence of Todd's paralysis, and the past. Among the idiopathic cases, ke-and-wave electroencephalographic rovoked seizures in the past, and a n patients with idiopathic causes and % still had recurrence at 5 years after orst prognosis—80% recurrence at 5 s and provoked seizures in the past. udy, a retrospective population-based ence rate—56% by 5 years.[3] Again, was no previous neurologic insult. ociated with higher recurrence rates ies, and abnormal findings on neuro- h previous neurologic insults, focal c factor.

aled that the overall risk of recurrence 2% at 4 years after a first unprovoked urologic insults, the risk of recurrence d seizure was a focal seizure or when Among children whose first seizures vas increased by the presence of EEG first-degree relatives was also a risk nal EEG results. Children whose first l normal EEG results had the best 3% at 2 years. However, the risk at 2 were abnormal. Similar to the pattern occur within 1 year after the first

ent should not be based solely on the clinician and the patient should also l, and psychologic consequences of , an adult who drives for a living may or her first seizure was a generalized t warning. Alternatively, the Commit- y of Pediatrics does not recommend st unprovoked seizure.[1] Also, initial sy syndromes in childhood may not res in these syndromes may not be eous remission may be good (such as eful counseling and guidance by the to the patient and to the guardian. ture recurrent (for example, absence oregoing studies specifically excluded should make certain that the seizure unprovoked seizure ever experienced.

Careful interview may sometimes disclose a history of previous seizures. Some patients presenting with generalized convulsions may neglect to report past occurrences of less dramatic partial seizures. The risk of another seizure after two unprovoked seizures is more than 65%, and most such patients have multiple seizures.[16] These patients have epilepsy, and AED therapy is necessary in most cases. Table 1 outlines the steps to follow when considering treatment of the first seizure.

OPTIMIZING SINGLE-DRUG THERAPY

With AED therapy, both clinicians and patients expect seizures to become fully controlled. Unfortunately, despite adjustments and modifications of their medications, a third of patients will not experience long-term remission (at least 5 years). The most important predictor of a patient becoming seizure-free is the duration of epilepsy history.[2] The longer patients continue to have seizures, the less likely it is that their epilepsy will remit. The first 2 years of treatment appear to be critical in determining long-term outcome.[12] If seizures are not controlled during this period, the likelihood of becoming seizure-free diminishes. Although the failure of seizures to respond promptly to treatment may be a reflection of severe epilepsy, it behooves clinicians and patients to optimize AED therapy early in the course of epilepsy. Educating patients about the importance of prompt control of seizures may also enhance compliance.

Several AEDs are available for the treatment of partial epilepsies. The most commonly used have been carbamazepine, phenobarbital, phenytoin, and primidone. For many years, no scientific information was available to determine which of these four drugs should be used first for the treatment of partial epilepsies. In the mid-1980s, a landmark multicenter study addressed this issue.[20] Both seizure control and adverse effects were objectively assessed in this randomized, double-blind study of adults with newly diagnosed partial epilepsy. Efficacies of the drugs studied were determined by composite scores that reflected both the degree of seizure control and the severity of adverse effects. Assessment was also based on the duration during which patients were

Table 1. STEPS TO FOLLOW WHEN CONSIDERING ANTIEPILEPTIC DRUG TREATMENT AFTER A FIRST SEIZURE

First Seizure		
Provoked	*Unprovoked*	
	Adult	*Child*
Consider whether provoking factor can be corrected If yes, AED treatment is unnecessary If no, AED treatment should be considered	Estimate recurrence risk Assess consequences of recurrence (medical, social, occupational, psychologic) Consider patient's preference Consider whether benefits outweigh risks If yes, advise AED treatment If no, withhold AED treatment	No AED treatment unless consequence is grave

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