

PERSPECTIVES IN PEDIATRIC NEUROLOGY

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PERSPECTIVES  
IN PEDIATRIC NEUROLOGY

EDITORIALS, ESSAYS, INTERVIEWS,  
ARTICLES, ABSTRACTS, AND  
COMMENTARY ON A BROAD RANGE  
OF TOPICS IN CHILD  
NEUROLOGY

P E R S P E C T I V E S I N  
PEDIATRIC NEUROLOGY

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IN THIS ISSUE:  
ABSENCE SEIZURES AND SYNDROMES:  
AN OVERVIEW WITH CASE STUDIES

VOLUME THREE

NUMBER ONE



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This activity is designed to respond to the needs  
of neurologists, pediatricians, and other physi-  
cians who treat children with seizures.

## Educational Objectives

After reading this monograph and completing  
the post-test, the participant should be able to:

- Describe the pathophysiology of absence  
seizures
- Describe the clinical and EEG characteristics  
of typical and atypical absence seizures
- Outline and describe the epidemiology and  
natural histories of epilepsy syndromes that  
include absence seizures
- Better diagnose absence seizures and select  
appropriate drugs for treatment

## Statement of Educational Method

The educational information is presented in a  
12-page monograph.

## Statement of Evaluation Instrument

A 12-question multiple-choice post-test is  
used as the evaluation instrument. An activity  
evaluation questionnaire will be completed by  
each participant.

## Statement of Intended, or Target, Audience

This activity is intended for, but not limited to:  
pediatric neurologists, pediatricians, and other  
physicians who care for children with epilepsy.

## Instructions

To earn 1 hour of category 1 credit, read the  
material in this monograph carefully. Complete  
the activity evaluation and answer the post-test  
questions on the accompanying questionnaire.  
Send the questionnaire in the enclosed envelope  
to: Virginia Commonwealth University,  
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Office of Continuing Medical Education,  
P.O. Box 980048, Richmond, VA 23298-0048.  
ATTN: ABSENCE SEIZURES PROGRAM.  
Your credit certificate will be returned.  
Participation is confidential. Estimated program  
completion time: 1 hour.

Course Number: END 0011 101 01

Release date: 11-01-01  
Expiration date: 10-31-03

## Answer key to CME Post-Test

1. D 2. A 3. B 4. D 5. D 6. A 7. A 8. C  
9. E 10. A 11. A 12. C

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## FROM THE EDITOR

Absence Seizures and Syndromes:  
an Overview

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During the 1970s, Kiffin Penry and his colleagues conducted landmark studies of absence seizures, describing their characteristics in great detail.<sup>1</sup> Nevertheless, as the two case studies in this issue of *Perspectives in Pediatric Neurology* illustrate, absence seizures may continue to elude diagnosis. This often occurs because the manifestations of absence seizures can be both subtle and very brief. They are often mistaken for daydreaming. On the other hand, absence seizures with unusual or dramatic automatisms might lead to a misdiagnosis of complex partial seizures. Furthermore, as one of the cases shows, a focal-onset seizure that rapidly generalizes into an apparent absence seizure may be misdiagnosed (and inappropriately treated) as a primary generalized seizure. In still other instances, patients may have brief, unrecognized absence seizures that progress to generalized tonic-clonic seizures (GTCS). As a result, the patient receives a drug for GTCS that fails to control, and may even worsen, the absence seizures.<sup>2</sup> One of Penry's favorite anecdotes concerned a teenaged girl whose absence seizures went undetected until she obtained her driver's license. With her mother in the passenger seat, she drove through a red light at an intersection, striking another car. When her astonished mother asked her daughter what happened, the girl had no memory of the event. Thus, what had been dismissed as "daydreaming" for many years turned out to be frequent absence seizures; it took a serious accident for her to be referred for diagnosis.

*Pathophysiology and clinical characteristics of typical absence seizures*

While the pathophysiology of absence seizures has not been definitively established, it is generally believed that inhibitory phenomena are involved in ictal events. Absence seizures may be a response of an abnormal neocortex to synchronizing input from the brain stem and thalamus.<sup>3</sup>

Typical absence seizures are primary generalized seizures characterized by brief staring episodes, lasting two to 15 seconds (generally less than 10 seconds), with impaired consciousness and responsiveness. They begin without warning (no aura) and end suddenly, leaving the person alert and without postictal confusion. Often, the person will resume preattack activities, as if nothing had happened.<sup>2</sup> Simple absence seizures are characterized by staring spells alone. In complex absence seizures, which are more common, staring is accompanied by automatisms, such as eye blinks or lip smacking; they may include mild clonic, atonic, or autonomic components involving the facial muscles. There may also be a slight nod of the head or semi-purposeful movements of the mouth or hands. The automatisms tend to be stereotyped, with the same behaviors occurring during each seizure. Penry et al observed automatisms in 63% of all absence seizures.<sup>2</sup> However, the automatisms are less elaborate than those observed with complex partial seizures. There may also be autonomic

**TABLE 1. Classification of absence seizures**  
(from Pearl and Holmes)<sup>4</sup>

## Typical absence seizures

- Simple: impairment of consciousness only
- Complex: with mild clonic components  
with changes in tone  
with automatisms  
with autonomic components
- Atypical absence seizures
- Absence status

manifestations, such as pupil dilation, flushing, tachycardia, piloerection, salivation, or urinary incontinence.<sup>3</sup> Absence seizures are classified in Table 1.

Absence seizures can be provoked by one or two minutes of hyperventilation and may be terminated by a loud or repetitive stimulus. Sleep deprivation, drowsiness, and photic stimulation may also precipitate seizures. Total sleep deprivation may elicit absence seizures even in children who have been seizure-free for many years on medication.<sup>2</sup> Children who are active and happy experience fewer seizures than those who are anxious, inactive, or bored.<sup>5</sup>

Onset of absence seizures is usually between the ages of five and 10; they never occur prior to age 2 1/2 and onset is rare after age 20.<sup>6</sup> Approximately 25% of affected children experience their first seizure before the age of five and 67% between the ages of five and 15. Fifty percent of patients will experience a remission of seizures following adolescence.<sup>2</sup> Forty to fifty percent of patients with recurring absence seizures will also experience one or more generalized tonic-clonic seizures.<sup>2,7</sup> In 14% of patients with *childhood absence epilepsy*, the disorder begins with both absence and GTCS.<sup>8</sup> Generalized tonic-clonic seizures are seen less often in children with an early onset of absence seizures. The prognosis is better for a child who experiences typical absence seizures alone, without other seizure types.<sup>9</sup>



FIGURE 1.

EEG pattern of typical absence seizure

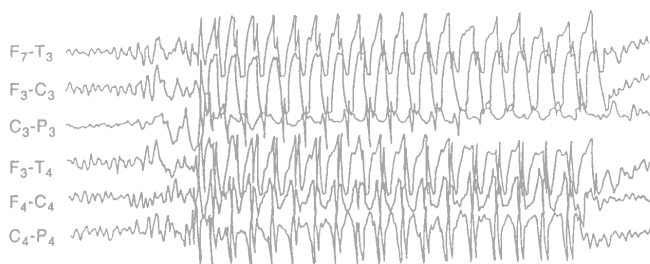
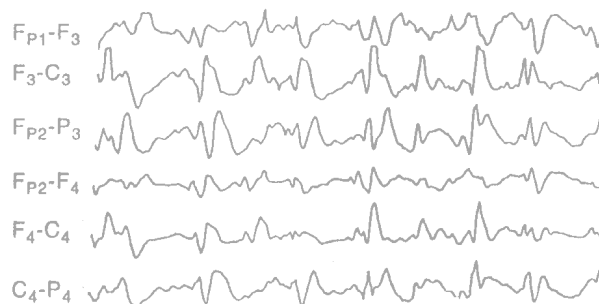


FIGURE 2.

EEG pattern of atypical absence seizure



On the EEG, typical absence seizures are associated with generalized, bilaterally synchronous, frontally predominant 3 Hz spike-and-wave discharges that begin suddenly from a normal background and end abruptly, without postictal slowing (Figure 1).<sup>3,10</sup> Interictal discharges do not occur.<sup>8</sup>

### Atypical absence seizures

Atypical absence seizures usually occur in children with below average intelligence. They are often related to diffuse or multifocal structural lesions in the brain.<sup>3</sup> Seizures usually last longer than 10 seconds, begin and end more gradually than typical absence seizures, and are not precipitated by hyperventilation. During an atypical absence seizure, consciousness may be only partially impaired and it may be difficult to distinguish the seizure from the child's usual behavior. Atonic attacks with complete collapse, rather than head nodding, often occur. These patients often have histories of clusters of generalized tonic-clonic seizures<sup>2</sup> and they have a greater tendency to develop absence status than those with typical absence seizures.<sup>3</sup> On the EEG, atypical absences are associated with poorly organized and irregular spike-and-wave discharges of 1 to 2.5 Hz (Figure 2). The primary differential diagnosis for both typical and atypical absence seizures is complex partial seizures; their characteristics are compared in Table 2.

### Absence status

In absence status, one staring spell follows another without complete recovery between spells. The person wanders in a fugue state, only semi-responsive to questions and performing poorly on tasks. Approximately 10% of children with absence seizures will experience at least one episode of absence status.<sup>11</sup>

### Absence syndromes

Typical absence seizures occur in three generalized idiopathic epilepsy syndromes; these are listed in Table 3 along with three generalized symptomatic epilepsy syndromes that include absences. The idiopathic syndromes, *childhood absence epilepsy*, *juvenile absence epilepsy*, and *juvenile myoclonic epilepsy*, appear to be genetically distinct, but there is some clinical and electrographic overlap among them. It has also been noted that *childhood absence epilepsy* will occasionally evolve into *juvenile myoclonic epilepsy*.<sup>10</sup> *Childhood absence epilepsy* (CAE), also known as *petit mal epilepsy* or *pyknolepsy*, is characterized by typical absence seizures in children who are apparently otherwise normal. "Pyknos" is Greek

for crowded clusters, referring to the tendency of children with this syndrome to experience clusters of a few to several hundred absences per day.<sup>7,8</sup> While children with this syndrome have no associated neuropathologies,<sup>12</sup> they may have cognitive deficits related to the underlying syndrome. Certainly, it is easy to understand how several hundred absences per day can interfere with cognitive functioning. A classic example of a learning disability caused by the seizures themselves is the child who has a flurry of absence seizures during the school day. The teacher notes that she is inattentive or appears to be daydreaming, while she is actually having dozens of brief, generalized seizures that impair her consciousness and make sustained learning difficult. Every year, the epilepsy clinic on VCU's Medical College of Virginia Campus sees a few children who appear to have Attention Deficit disorder but actually have absence seizures. It isn't cost effective to perform an EEG on every child who has a learning disability in order to detect the few who have seizures. Fortunately, uncomplicated absence seizures are associated with a good prognosis for cognitive functioning once seizures are controlled. In the example above, it was attention, rather than cognition, that was impaired by the seizures. However, a recent study conducted detailed neuropsychological testing in 16 children with CAE and 16 well-matched children without epilepsy. Of the 16 patients with CAE, 11 were treated with valproate monotherapy, two with

*Total sleep deprivation may elicit absence seizures in children who have been seizure-free for many years on medication.*

**TABLE 2.**

Differential diagnosis: Typical absence, atypical absence, and complex partial seizures

	Typical absence seizures	Atypical absence seizures	Complex partial seizures
<b>Aura</b>	Never	Rare	Often
<b>Automatisms</b>	Less elaborate	May be more elaborate	More elaborate
<b>Mean duration</b>	Usually < 10 sec	Any duration (usually > 10 sec)	Usually > 10 sec
<b>Postictal confusion</b>	No	Possibly	Yes
<b>Ictal EEG</b>	Synchronous 3 Hz or faster spike-and-wave	Atypical spike-and-wave, usually 2.5 Hz or slower	Focal spikes
<b>Mental status</b>	Normal	Low IQ	Usually normal
<b>Prognosis</b>	Good	Poor	Variable

ethosuximide monotherapy, and three with both drugs. The researchers found similar, impaired neurocognitive profiles among the children with CAE; they had lower scores on measures of general cognitive functioning, visuospatial skills, and memory compared to controls, but with little impairment of verbal skills. The authors note that it is unlikely that anticonvulsant drug effects account for the cognitive deficits seen.<sup>13</sup>

*Childhood absence epilepsy* accounts for approximately 8% of childhood epilepsies and the majority of those affected are female. About one-third of affected children have a family history of epilepsy, while siblings of those affected have a 10% risk of experiencing seizures.<sup>7</sup> While an autosomal dominant gene with age-dependent penetration has been identified for CAE, some degree of brain damage may be necessary to trigger the disorder.<sup>14</sup>

*Juvenile absence epilepsy* is much less common than the childhood form, and males and females are affected equally. In *juvenile absence epilepsy*, absence seizures begin at or after puberty but they occur less frequently than in childhood absence epilepsy. Absence status and generalized tonic-clonic seizures are more likely to occur in this syndrome and patients may also experience myoclonic seizures.<sup>3</sup> *Juvenile absence epilepsy* is associated with spike-and-wave discharges of 3 Hz or faster.<sup>10</sup> Absence seizures also occur in *epilepsy with generalized tonic-clonic seizures on awakening*<sup>3</sup> and in approximately 25% of patients with *juvenile myoclonic epilepsy*.<sup>15</sup> Atypical absence seizures are characteristic of *Lennox-Gastaut syndrome*.<sup>3</sup>

**TABLE 3.**

Absence syndromes (from Pearl and Holmes)<sup>4</sup>

Generalized idiopathic epilepsies	Generalized symptomatic epilepsies
<ul style="list-style-type: none"> <li>■ Childhood absence (pyknolepsy)</li> <li>■ Juvenile absence</li> <li>■ Juvenile myoclonic</li> </ul>	<ul style="list-style-type: none"> <li>■ Lennox-Gastaut syndrome</li> <li>■ Epilepsy with myoclonic atstatic seizures</li> <li>■ Epilepsy with myoclonic absences</li> </ul>



## Prognosis

Several factors influence the prognosis of a patient with absence seizures. Patients who have no apparent acquired brain lesion and whose epilepsy is primarily genetic in origin (e.g., those with *childhood absence epilepsy*) generally have a good prognosis. Early onset of absence seizures and rapid response to medication are also good prognostic signs.<sup>3</sup> By contrast, patients with absence seizures associated with brain lesions, mild retardation, abnormal background activity on the EEG, and atypical spike-wave discharges (e.g., those with Lennox-Gastaut syndrome) have a poorer prognosis.

## Drug Therapy

Typical absence seizures are remarkably responsive to treatment; fewer than 5% of cases are refractory.<sup>2</sup> The drugs of choice for *childhood absence epilepsy* and *juvenile absence epilepsy* are ethosuximide or valproate. The latter is preferable if the patient also has GTCS or if the physician wishes to reduce the risk of future GTCS.<sup>14</sup> Valproate may be more effective than ethosuximide for atypical absence seizures.<sup>3</sup> Ethosuximide is given at a dose of 20 to 40 mg/kg daily, to achieve serum levels of 40 to 100 µg/mL. The side effects of ethosuximide include anorexia, nausea, vomiting, headaches, lethargy, and dizziness. Valproate is given at a dose of 20 to 60 mg/kg, to achieve a level of 50 to 100 µg/mL. The side effects of valproate include tremor, weight gain, and transient hair loss.

## Remission and drug withdrawal

Absence seizures associated with *childhood absence epilepsy* tend to remit in adolescence; complete remission occurs in approximately 50% of patients. If the patient has none of the signs listed above suggesting a poor prognosis, the rate for complete remission rises to 90%. The absence seizures associated with *juvenile absence epilepsy* are less likely to remit spontaneously, although response to medication is good.<sup>3</sup>

Because typical absence seizures tend to remit in adolescence, an attempt should be made to withdraw medication after a seizure-free period of approximately four years. Tapering should be very slow, over six months to one year.<sup>3</sup>

In summary, it can be very gratifying to treat children with typical absence seizures, because the vast majority will respond to medication. As early as 1984, Penry noted that "No form of epilepsy is easier to treat than absence seizures."<sup>2</sup> He added that, unfortunately, many patients with absence seizures remain uncontrolled, usually due to incomplete diagnosis, a situation that remains true today. The following two cases are compelling illustrations of how incomplete diagnoses led to initial difficulties that were later overcome through a careful reconsideration of the initial diagnoses. ■

*Early onset  
of absence seizures and  
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prognosis.*



## References

1. Penry JK, Porter RJ, Dreifuss FE. Simultaneous recording of absence seizures with video tape and electroencephalography. A study of 374 seizures in 48 patients. *Brain*. 1975;98:427-440.
2. Penry JK. Diagnosis and treatment of absence seizures. *Cleve Clin Q*. 1984;51:283-286.
3. Engel J Jr. *Seizures and Epilepsy*. Philadelphia: FA. Davis Company, 1989.
4. Pearl PL, Holmes GL. Absence seizures. In: Pellock JM, Dodson WE, Bourgeois BF (eds). *Pediatric Epilepsy: Diagnosis and Therapy*, 2nd ed. New York: Demos Publications, 2001.
5. Guey J, Bureau M, Draver C, et al. A study of the rhythm of petit mal absences in children in relation to prevailing situations. The use of EEG telemetry during psychological examinations, school exercises and periods of inactivity. *Epilepsia*. 1969;10:441-451.
6. Treiman DM. Seizure types and causes of epilepsy. *Seminars in Neurology*. 1981;1(2):65-75.
7. Berkovic SF. Childhood absence epilepsy and juvenile absence epilepsy. In: Wylie E (ed). *The Treatment of Epilepsy: Principles and Practice*. Philadelphia: Lea & Febiger, 1993.
8. Delgado-Escueta AV, Treiman DM, Walsh GO. The treatable epilepsies. *N Engl J Med*. 1983;308:1508-1514.
9. Sato S, Dreifuss FE, Penry JK. Prognostic factors in absence seizures. *Neurology*. 1976; 26:788-796.
10. Berkovic SF, Andermann F, Andermann E, et al. Concepts of absence epilepsies: Discrete syndromes or biological continuum? *Neurology*. 1987;37:993-1000.
11. Porter RJ, Penry JK. Petit mal status. In: Delgado-Escueta AV, Wasterlain C, Treiman DM, Porter RJ (eds). *Status epilepticus: Mechanism of Brain Damage and Treatment*. New York: Raven Press, 1983.
12. Murphey JV. Valproate monotherapy in children. *Am J Med*. 1988;84 (Suppl 1A):17-22.
13. Pavone P, Bianchini R, Trifiletti RR, et al. Neuropsychological assessment in children with absence epilepsy. *Neurology*. 2001;56(8):1047-1051.
14. Loiseau P, Pestre M, Dartigues JF, et al. Long-term prognosis in two forms of childhood epilepsy: Typical absence seizures and epilepsy with rolandic (centrotemporal) EEG foci. *Ann Neurol*. 1983;13:642-648.
15. Dreifuss FE. Juvenile myoclonic epilepsy: Characteristics of a primary generalized epilepsy. *Epilepsia*. 1989;30 (Suppl 4):S1-S7.

### Correction

In *Perspectives in Pediatric Neurology*,  
Volume Two, Number Two,  
there were two errors of attribution in  
the article entitled "Learning disabilities in  
children with epilepsy."

1. The reference for Figure 1 was  
inadvertently omitted.

It is: Dodson WE. *Epilepsy and IQ*.

In: Dodson WE, Pellock JM (eds).

*Pediatric Epilepsy: Diagnosis and Therapy*.

New York: Demos Publications, 1993.

2. Table 1 should have been labeled

"from Dodson," rather than

"adapted from Dodson." Table 1 was also

mistakenly attributed to the 2001 edition

of *Pediatric Epilepsy: Diagnosis and Therapy*

instead of the 1993 edition.

The editor regrets the errors.

### CASE REPORT

## A five-year-old girl with staring spells that worsened after treatment

Anthony R. Riela, M.D.  
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**When the dose  
was raised a third time,  
surprisingly, her spells  
worsened.**



Brenda G. is a five-year-old girl from a suburb of Dallas who presented with a history of staring in her first year of school. These staring spells lasted about 30-40 seconds. Initially, these spells occurred a couple of times a week. Sometimes, she would recover quickly and go back to what she was doing before the episode. Other times, she was confused for 5-10 seconds, after which she would return to her previous activity. After she experienced these spells for two months in school, her teachers thought that she had Attention Deficit disorder. Eventually, these spells came to the attention of her pediatrician.

Brenda's history was otherwise uneventful. She was the product of a full-term pregnancy and had no problems around the perinatal period. Her development was normal and she was doing fine in kindergarten. While the staring spells were first noticed in the beginning of her kindergarten year, they may have been present earlier. Her pediatrician saw her about three months into the school year. He considered the possibility of a seizure disorder and did an EEG, which showed a normal background, but also a kind of asymmetric spike-and-wave pattern, predominantly on the left side. During sleep, the focal spikes sometimes generalized, but there were frequent, independent left and right spikes in the frontal area.

The physician who read the EEG was an adult neurologist. He thought the pattern was consistent with seizures and suggested that these may be complex partial seizures. Brenda was started on carbamazepine. Initially, she appeared to have improved somewhat on medication, but continued to have occasional staring spells.



A blood test to check the carbamazepine level showed it to be on the low side, so her dose was increased. After the dose increase, the number of staring spells increased. The blood level was re-checked and shown to be still low, so it was raised again. At this time, her serum carbamazepine level was about 6 µg/mL (therapeutic range: 4-12 µg/mL).

Because Brenda kept having staring spells and the drug level remained low, the dose was raised a third time. Surprisingly, her spells worsened. Sometimes they lasted a minute or more and were associated with longer periods of confusion afterwards. Then she started having new spells, where she would fall to the floor in an apparent drop attack. As the family described it, she would suddenly “get limp.” After having been on an anticonvulsant about 6 or 8 weeks, her situation had noticeably worsened. In effect, she had so many staring spells and drop attacks that she became non-functional. She had trouble eating and eventually ended up in the emergency department. That’s when we saw her for the first time.

On exam, we found that she was encephalopathic, with many staring events. We put her in our epilepsy monitoring unit, where we found she was having very frequent spike-and-wave discharges. It was not the classic 3 Hz spike-and-wave; it was a little slower, at 2-3 Hz and, although generalized, it was slightly asymmetric, with more activity on the left side.

While she was being monitored, Brenda had several seizures. While she was still in the monitoring unit, we stopped the carbamazepine, and the EEG improved. She developed the classic, 3 Hz, spike-and-wave pattern of absence epilepsy, but the EEG was still a little asymmetric. We started her on Depakote® Sprinkle (divalproex sodium coated particles in capsules), titrated to 125 mg t.i.d. Soon after discharge, she improved but still had occasional staring spells.

However, when she came for follow up in three weeks, we learned that her seizures had stopped about the third or fourth day after leaving the hospital, which was a little over a week after stopping the carbamazepine. Since then, she has been seizure-free. When we first evaluated her, we couldn’t assess her mental status because she was so encephalopathic. As it turned out, her mental status was normal after her seizures were controlled.

### **Discussion**

This scenario is not an unusual one. Brenda probably has classic absence seizures, but atypical features led to an initial misdiagnosis. Her first EEG did not show the classic bilaterally synchronous and symmetrical, 3Hz, spike-and-slow-wave pattern. The adult neurologist who read the EEG found the pattern, which was somewhat asymmetrical and frontally predominant, to be more consistent with complex partial seizures (CPS). He prescribed carbamazepine, an appropriate agent for CPS, but inappropriate for absence seizures.

**An EEG  
showed a normal background  
and an asymmetric spike and wave  
pattern, predominantly  
on the left side.**



There is a lesson here that applies to any patient with poorly controlled seizures. No matter how long ago the diagnosis was established, it is frequently very useful to go back to “square one” and re-establish the diagnosis. With Brenda, our suspicions were raised by her history of worsening seizures on carbamazepine; indeed, the degree of worsening seemed to be dose-related. There have also been reports in the literature of carbamazepine-related drop attacks. It seemed very probable that the initial diagnosis of CPS was wrong and that her treatment was responsible for her worsening condition. Our experience with Brenda in the epilepsy monitoring unit confirmed our suspicions, and Brenda was discharged on Depakote® Sprinkle, a first-line drug for absence seizures.

What about the drop attacks? Were they atonic seizures or a drug-related manifestation of absence? As Kiffin Penry showed with his early video studies of absence seizures, our conception of absence seizures as simply staring spells is too limited. He demonstrated that only about 10% of absence seizures consist of stares only. Most include other features, such as automatisms, increased muscle tone or, as in Brenda’s case, a loss of tone. So it is most likely that the drop attacks were a manifestation of her absence seizures brought out by carbamazepine.

Brenda has been followed for a year and a half and is still seizure-free. A follow-up EEG six months after discharge was normal. After she has been seizure-free for about two years, we will take another look at her EEG and, if it remains normal, attempt to withdraw her medication. Typically, we taper the drug over a two-to four-week period as soon as school lets out, so we have the summer to see if any relapses occur. About two-thirds of children with absence epilepsy will remain seizure-free after drug withdrawal. In summary, Brenda’s prognosis is excellent. ■

CASE REPORT

A nine-year-old-girl  
with intractable absence seizures  
and a possible focal lesion

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The Lorna S. and James P. Langdon  
Chair of Pediatric Epilepsy  
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Ellen G. is a nine-year-old girl who initially presented with what appeared to be typical absence seizures. During the previous several months she had repeated stereotyped attacks characterized by staring and unresponsiveness, which lasted several seconds. She was amnesic for test items presented during the seizures. The episodes usually lacked any motor manifestations, although her father, after repeated interviews, believed that on a few occasions he may have seen some subtle deviation of her eyes and perhaps subtle tonic posturing of one arm.

Early development was normal and there were no risk factors for epilepsy. She was in a 4th-grade class with 32 children and had a history of mild learning disabilities going back to the first or second grade. Her parents complained of some difficulties with her current school performance.

General physical and detailed neurological examinations were normal. Hyperventilation for 1 minute and 45 seconds induced a typical absence seizure lasting approximately 10 seconds.

Routine EEGs, obtained while she was awake and hyperventilating, revealed highly stereotyped 3 Hz spike-wave discharges with a generalized distribution. The electrographic findings were interpreted as being consistent with childhood absence epilepsy.

MRI revealed a small hyperintense signal on T2-weighted scans in the left globus pallidus. The clinical significance of this abnormality was uncertain, and repeat imaging six months later showed no change in the lesion.

She was treated with divalproex sodium with doses as high as 45 mg/kg/day. Her parents noted a change in her personality during this time, but it was not clear whether it was related to the medication. Attacks continued, so the medication was withdrawn. Ethosuximide was begun, but low doses caused stomach upset and her parents requested a change of medication.



*he findings were  
consistent with a form  
of localization-related  
epilepsy with rapid  
secondary generalization,  
mimicking typical  
absence epilepsy.*

Video EEG monitoring revealed a normal background with a well-developed and modulated 9 Hz alpha rhythm. The most conspicuous feature of the recording was the presence of numerous bursts of generalized spike-wave discharges with a repetition rate of 3 Hz (Figure 1). These discharges were more prominent in the frontal derivations and sometimes had polyphasic components. The discharges lasted 5-10 seconds and were accompanied by unresponsiveness and amnesia for test items. There were no motor manifestations or automatisms associated with the discharges. Careful scrutiny of the discharges revealed other interesting features. By altering the "paper speed" of the display to 60 cm/sec and adding a channel comparing F3 to F4, one could appreciate a subtle, left-hemisphere lead-in to many of the discharges (Figure 2).

We concluded that these findings were consistent with a form of localization-related epilepsy with rapid secondary generalization, mimicking typical absence epilepsy. Based on these findings, gabapentin was begun, but seizures worsened. She was switched to acetazolamide, which resulted in a remarkable reduction of the seizures. Alternative medications currently under consideration are lamotrigine and zonisamide.

FIGURE 1.

Conventional speed EEG, showing repetitive spike-wave discharges with a diffuse distribution and a frontal maximum

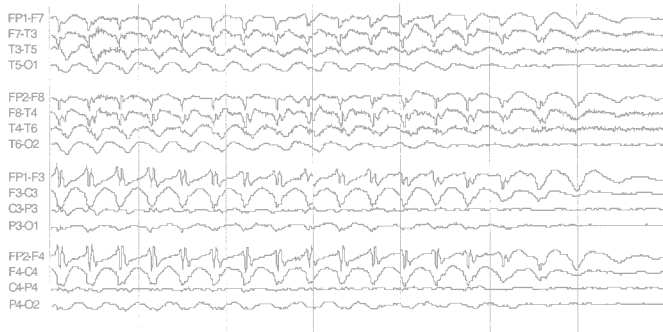
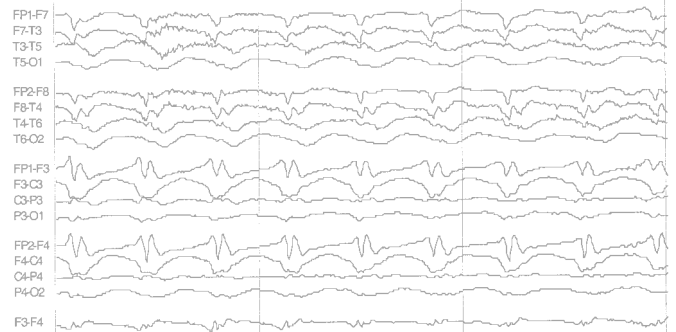


FIGURE 2.

"Fast" EEG, showing subtle lead-in from the left hemisphere, especially in the F3-F4 channel



## Discussion

This patient presented with what appeared to be absence seizures, which proved refractory to classic absence medications. The question then becomes: is this a case of refractory absence epilepsy, or was the initial diagnosis incorrect? There are new agents available that may have some efficacy in refractory absence seizures. There are reports from Japan, for example, on refractory absence seizures with focal features that were treated with zonisamide with good results.

There are rare genetic causes of intractable absence that might be considered, such as glucose-transported protein defect and a condition involving hyperaminemia and hypoglycemia. Another possibility is that the abnormality in the left globus pallidus seen on the MRI may be related to a structural anomaly somewhere in the cortex that is the source of the seizures.

The lesson here is that, in patients who don't respond to appropriate therapy for their seizure type, one should consider alternative diagnoses. This patient was treated unsuccessfully with drugs for generalized seizures that work in the vast majority of patients with absence; this was a cue for consideration of a diagnosis other than absence.

Based on the rather subtle EEG findings, it was concluded that this patient has complex partial seizures with rapid secondary generalization. She remains on acetazolamide at only 10 mg/kg/day and is remarkably improved, with a marked reduction in seizure frequency. It should be noted, however, that this is a short-term follow up, only a couple of weeks after initiating therapy. Acetazolamide is notorious for having short-lived efficacy in some patients. Some patients have done well long term on acetazolamide, but often it remains effective for only a brief period. It is possible that Ellen will require some other agent long term, perhaps something in combination with divalproex sodium or an alternative AED like lamotrigine or zonisamide. Once she is clinically in remission, objective data will be obtained on seizure frequency.

A noteworthy feature of this case is the extremely rapid secondary generalization. It was so rapid, in fact, it could only be appreciated at the equivalent of a paper speed of 60 cm/sec and by using a technique with the EEG electrodes that originated in a report in the *Journal of Clinical Neurophysiology*. One of the frontal electrodes, for example F3, is plugged into one of the channels, for example Grid 1. F4 is then plugged into the other channel, for example Grid 2. The signal is then passed through the EEG machine. Since the EEG is basically a differential amplifier, one then exam-

ines the differences between the signals. If the signal were hitting the frontal regions precisely on time, completely synchronized and at the same amplitude, then the difference between the F3 and F4 signals would be zero; there would be a straight line. In other words, if the seizure were a pure, generalized discharge, it should produce a straight line under these conditions. If the amplitude is higher in one channel or the other, the line would be skewed slightly in the direction of the higher amplitude. But if the signal is starting in one one place and secondarily generalizing, there would be a more complex tracing in the combined F3 to F4 channel. The latter is, in fact, what was seen on this patient's EEG: a wave form that looked more complex than the signal at either channel independently. This was very suggestive of a partial seizure with very rapid secondary generalization.

What about Ellen's prognosis? Because a focal lesion appears to be responsible for the seizures, she may be a candidate for surgery. A repeat MRI was done; we looked very carefully at the region above the globus pallidus to see if any abnormality could be visualized in the adjacent cortex or overlying cortex, but unfortunately none was apparent. Nevertheless, this patient is a potential candidate for epilepsy surgery, particularly if the spells continue to be difficult to control with medications and if we can ultimately visualize the lesion on imaging. ■

## POST-TEST QUESTIONS

Eight correct answers are required for a passing score

- Which of the following may occur during a complex absence seizure?  
 A. Mild tonic or atonic components  
 B. Stereotyped automatisms, such as lip smacking  
 C. Pupil dilation and piloerection  
 D. All of the above  
 E. A. and B. above
- The prognosis is better for a child who experiences absence seizures alone, without other seizure types.  
 A. True  
 B. False
- What percentage of children with absence experience their first seizure before age 5?  
 A. 50%  
 B. 25%  
 C. 75%
- Which of the following may precipitate a typical absence seizure?  
 A. Photic stimulation  
 B. Drowsiness  
 C. Hyperventilation  
 D. All of the above
- What percentage of children with recurring absence seizures also experience GTCS?  
 A. 10-20%  
 B. 20-30%  
 C. 30-40%  
 D. 40-50%
- The earlier the onset of absence seizures, the less the likelihood of GTCS also occurring.  
 A. True  
 B. False
- Valproate may be more effective than ethosuximide in controlling atypical absence seizures.  
 A. True  
 B. False
- If the patient has no risk factors for a poor prognosis, what is the remission rate for absence seizures during adolescence?  
 A. 50%  
 B. 75%  
 C. 90%
- How do atypical absence seizures differ from typical absence seizures?  
 A. They are associated more often with focal or diffuse brain lesions  
 B. They begin and end more gradually  
 C. They are not elicited by hyperventilation  
 D. Atonic attacks may occur  
 E. All of the above
- Which of the following EEG patterns is characteristic of atypical absence seizures?  
 A. Irregular, poorly organized spike-and-wave discharges of 1-2.5 Hz  
 B. Bilaterally synchronous, frontally predominant 3 Hz spike-and-wave discharges  
 C. Generalized poly spike-and-wave pattern
- What percentage of children with absence seizures will experience at least one episode of absence status?  
 A. 10%  
 B. 25%  
 C. 40-50%
- Which of the following is a generalized symptomatic epilepsy?  
 A. Juvenile myoclonic epilepsy  
 B. Pyknolepsy  
 C. Lennox-Gastaut syndrome



## PERSPECTIVES IN PEDIATRIC NEUROLOGY

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Separate this form along perforation, fold, and mail in the enclosed envelope.



**POST-TEST ANSWERS**

Circle the appropriate letter for each question.

1. A. B. C. D. E.    2. A. B.    3. A. B. C.
4. A. B. C. D.    5. A. B. C. D.    6. A. B.    7. A. B.
8. A. B. C.    9. A. B. C. D. E.    10. A. B. C.
11. A. B. C.    12. A. B. C.

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1. As a result of the information contained in this activity, will you make any changes in your practice? Yes \_\_\_\_\_ No \_\_\_\_\_  
If yes, what changes? \_\_\_\_\_  
\_\_\_\_\_
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\_\_\_\_\_
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