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Management of Nonfebrile Seizures

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"Dr Robinson, help—Johnny's on the floor jerking—I think he's having a seizure!"

How often have you had a call similar to this? Because febrile seizures occur in 3% to 4% of your patients and nonfebrile seizures occur in 0.5% of children in your practice, calls like this must occur frequently.

What should you do for the parent on the phone? How should you help Johnny? Both are your patients, particularly at this time. A seizure is one of the most frightening things a parent can observe. What tests should you order? What can you tell the parent about the future? Should you treat and with what?

The approach to seizures (febrile and nonfebrile) has changed dramatically in the past 20 years. At one time, physicians were advised that phenobarbital therapy should be instituted for all children with a first seizure and therapy continued for the foreseeable future. For febrile seizures, that meant until they were 5 or 6 years old. For nonfebrile seizures, that meant forever, or at least until they were adults making their own decisions. Such teaching is out of date. The approach to *febrile seizures* has clearly changed, eliminating therapy for the vast majority of children.¹ Not all first afebrile seizures require treatment according to concepts of modern management. When treatment is instituted for a first or second seizure, it should be based on the type of seizure, the careful weighing of the risks of seizure recurrence, and the benefits and side effects of medication.² Careful attention must be paid to the cognitive and behavioral effects of anticonvulsant drugs, and they should be administered for the least time required.

Changes in the workup of patients with nonfebrile seizures have also occurred as new data and approaches to evaluation have become available.

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This article will update current thinking on the approach to the first nonfebrile seizure and its management.

WHAT DO YOU DO FOR MRS JONES ON THE PHONE?

Generalized tonic-clonic seizures are exceedingly frightening to everyone who witnesses them. The child arches his back (tonic), turns somewhat blue, and then begins the rhythmic (clonic) jerking. There is foam at the mouth. Many inexperienced observers are sure that the patient will die or, at least, swallow his tongue. The most important intervention at this point is reassurance that these things will not happen. An individual cannot swallow the tongue because it is attached to the back of the throat. The blueness comes during the tonic phase in which respiration is inhibited. In addition, skin circulation may decrease while blood goes to the head. However, if the patient becomes sufficiently hypoxic (a very rare event), the seizure will stop, and breathing will resume. Keeping the observers calm, having them turn the patient on his or her side, protecting him or her from sharp objects, putting something soft such as a pillow or a jacket under the head is all that is necessary. Most generalized tonic-clonic seizures last only a few minutes, and the ambulance need not be called. The patient should be observed for further seizures or other neurologic symptoms. An ambulance should be called *only* if a seizure lasts more than 15 minutes. If the seizure is still continuing when the child has been transported to the emergency room, then it has probably reached a limit of approximately 30 minutes (defined as status epilepticus) and should be treated with intravenous medication. There is *no* evidence that a seizure lasting less than 30 minutes produces permanent brain damage. There is evidence from animal experiments that a seizure lasting 30 minutes or longer *begins* to produce changes in the brain which, *if* continued, *might* result in permanent brain damage. Notice the italicized words. Education of parents

EDUCATIONAL OBJECTIVE

98. Appropriate ability to assess the risk of recurrent seizures after a single nonfebrile convulsion (Recent Advances, 86/87).

and others to these facts can markedly reduce the cost and inconvenience faced by people with epilepsy who are taken to an emergency room every time they have a seizure.

When the seizure has stopped by itself, commonly ending with a deep sigh, the patient is usually in a sleepy (postictal) state. This will last five to 15 minutes. When the patient wakes up, he or she may be confused and, therefore should be attended until he or she is alert and aware enough to return to work, home, or normal life.

Because status epilepticus is rarely the initial episode, the seizure would usually have stopped before the parent calls. If the seizure is continuing the first-aid measures described before will be helpful. Most pediatricians would want to see the child as soon as possible after the seizure to ensure that the child has returned to normal and that the episode is not a symptom of an acute disturbance affecting the CNS.

EVALUATION OF A FIRST SEIZURE

The most important aspect of the evaluation of a seizure is the history.³ There is *no* way to diagnose a seizure except by the correct interpretation of the events that occurred. Fortunately, with children, most events are observed by an adult who should be contacted for the detailed observation of what went on during the episode. The history is vital to differentiating seizures from other episodes that may alter consciousness in a

TABLE 1. Classification of Seizures

International Classification	Old Terminology
Partial seizures	Focal or local seizures
Simple partial seizures (consciousness not impaired)	
With motor symptoms	Jacksonian seizures
With somatosensory or special sensory symptoms	Focal sensory
With autonomic symptoms	
With psychic symptoms	
Complex partial seizures (with impairment of consciousness)	Psychomotor or temporal lobe seizures
Simple partial onset	
With impairment of consciousness at onset	
Partial seizures that secondarily generalize	
Generalized seizures (convulsive or nonconvulsive)	
Absence	Petit mal
Absence	
Atypical	
Myoclonic	Minor motor
Clonic	Grand mal
Tonic	Grand mal
Tonic-clonic	Grand mal
Atonic (astatic)	Akinetic, drop attacks

child, particularly fainting and breath holding, both of which may be accompanied by tonic-clonic movement. Both cyanotic and "pallid" breath-holding spells are common in children. Classic (cyanotic) breath-holding spells involve a prolonged expiration phase usually precipitated by crying. The child may become blue and sufficiently hypoxic to precipitate a brief tonic-clonic seizure. Pallid breath-holding spells are really a childhood form of vasovagal syncope and can often be simulated while monitoring the child by applying pressure to the eyeballs with production of a vagal discharge. The heart rate is slowed and an occasional period of brief asystole may be seen. Precipitating events such as fear, anxiety, hyperventilation, and crying should be sought. The history will also establish if the seizure was associated or concomitant with acute head trauma, possible hypoglycemia, infection, cardiac problems, or drug ingestion. No laboratory test can establish with certainty that a child had a seizure. Information about focality, incontinence, alterations or loss of consciousness, and the postictal

state may help to differentiate a true seizure from these other entities. The presence of fever in the appropriately aged child may help to separate febrile seizures from nonfebrile seizures. However, a seizure triggered by fever cannot be accurately separated from a febrile seizure until the individual goes on to have nonfebrile seizures.

After this careful and detailed history, the physician usually should be able to separate nonseizure events from true seizures. However, occasionally, one cannot be certain. If the child is otherwise doing well, it is far better to adopt an expectant attitude and wait and see whether the episode recurs. The parent can be educated to gather more specific information to better define the next event. This is more important than prematurely deciding that a child has had a seizure.

Classification of the different types of seizures is important to the clinician. There are certain types of seizures that will routinely recur. In addition, it is important to determine whether there is any element of focality because this implies the possi-

bility of a localizable abnormality within the brain. Certainly, it is also necessary to determine what type of seizure a child had in order to make a more logical choice of drug. Finally, there is evidence that prognosis for different types of seizures may be different. The current system divides seizures into partial (focal) and generalized (including absence and tonic-clonic seizures). The currently used terms are shown in parallel with the old terminology (Table 1).

A complete physical and neurologic examination is always mandatory. Seizures may be associated with systemic illness, renal disease, hypertension, or metabolic conditions. A careful neurologic examination should be performed both to detect focal neurologic deficit and to establish, when possible, whether this deficit is new or old. If new focal deficits are found, more immediate diagnostic evaluations should be performed. This examination should also form a baseline for follow-up examination to detect any evidence of a progressive neurologic deficit.

Which laboratory tests to obtain will depend on the history and physical examination findings (Table 2). There is *no* routine laboratory workup for the patient who has had a seizure. Because hypoglycemia and hypocalcemia can, on occasion, cause seizures without any otherwise detectable disease, we favor blood testing for glucose (after an overnight fast) and calcium levels. Tests for liver chemistries and a complete blood cell count are particularly useful as baseline evaluations before starting antiepileptic drugs.

An electroencephalogram (EEG) should be part of the initial workup of a patient with seizures (Table 3). However, an EEG does *not* provide evidence to diagnose a seizure unless a seizure occurs during the EEG. It is still the clinical description of an event that is important. Abnormal EEG results are compatible with seizures, as are normal EEG findings. One treats the patient with seizures, not the EEG. The EEG does, however, provide a baseline for further evaluation should the seizures become recurrent or change in pattern. Certain words in the EEG report are of special importance.⁴ *Focal slowing*

on the EEG is important because it usually indicates an acute focal disturbance. It does not tell you the type of disturbance. A finding of focal slowing is compatible with focal encephalitis, a stroke, a tumor, and other local disturbances. Focal slowing warrants further evaluation. *Focal spikes*, however, indicate a long-standing lesion and are of much less diagnostic concern. *Generalized slowing* may indicate an acute disturbance such as encephalopathy or may be long-standing. A *spike-wave* pattern on the EEG is, however, useful in distinguishing absence seizures (formerly referred to as petit mal) from other forms of epilepsy and from other conditions such as daydreaming. Spike-wave abnormalities can often be precipitated by hyperventilation.

If an EEG is to be performed, it should be complete and include hyperventilation, photic stimulation, and sleep (spontaneous or induced with hypnotic agents).

When should an EEG be performed in relationship to the seizure? Under ideal circumstances, it should be done during a seizure, but such serendipity is unusual. It would be of value to have an EEG immediately after a seizure to confirm postictal phenomena such as slowing. If slowing is seen, the EEG should also be repeated two or more days after the seizure to establish whether the slowing was related to a temporary physiologic disturbance or underlying anatomic abnormality. However, in general, we obtain a routine, complete EEG during the interictal state, several days to several weeks after the seizure.

Skull x-ray films are not useful in the evaluation of a patient who has had a seizure. Only if the seizure is related to trauma and one is worried about a depressed skull fracture should a skull film be performed. A computed tomographic (CT) scan is not a routine part of the initial workup for every child who has had a seizure. CT scans are far more useful than skull x-ray film in looking for intracranial abnormalities, tumors, or vascular problems, but these conditions are rare causes of epilepsy in children. We would reserve use of the CT scan for the child who has had a focal

TABLE 2. Laboratory Evaluation of Seizures

Test	Comment
Blood glucose Ca ²⁺	Fasting Occasionally helpful
Mg, PO ₄ , Na Complete blood cell count	Rarely helpful Consider as baseline
Liver function	Consider as baseline
Lumbar puncture	Consider—especially if possible infection or prodromal changes in behavior
Skull x-ray film Computed tomography	No Not routine—useful if clear focality
EEG	Yes—get complete study

slow-wave abnormal finding on the EEG, for one who has acquired focal deficit, or for the child who has continuing focal seizures. A CT scan may also be useful in the child whose seizure pattern is worsening or changing. To reiterate, a CT scan *need not* be obtained as part of the initial workup of the child who has had a seizure.

TO TREAT OR NOT TO TREAT

The decision to initiate therapy after a single seizure must include considerations of such factors as the age of the patient, the type of seizure, predisposing factors, the psychological and social consequences of further seizures, and the chance of recurrence of seizures. These risk factors should be weighed against the risks and consequences of the medication that will be used. These risks and consequences include the effects of medication on learning and behavior, the need to take daily medication, and the effect of labeling (Figure).⁵

In this discussion, we are concentrating on generalized tonic-clonic seizures and partial (focal) seizures. Absence seizures, myoclonic sei-

TABLE 3. Electroencephalogram Findings and Importance

Findings	Meaning
Focal slowing	Acute focal disturbance—encephalitis, stroke, tumor, etc
Focal spikes	Long-standing focal process
Generalized slowing	Acute or long-standing
Spike-wave	3/s seen in absence, slower pattern seen in atypical absence

zures and infantile spasms, are rarely seen at the time of the initial single seizure.

WHAT ARE THE RISKS OF RECURRENCE AFTER A SINGLE SEIZURE?

Among the first questions the parent asks are, "Why did he have a seizure?" and "Will it happen again?" Because more than half of childhood seizures are idiopathic, the likelihood of discovering the etiology for the seizures is small. Despite differing reported estimates of recurrence rates, due to variability in methodology, we are beginning to accumulate data that give us guidelines as to who is most likely to experience a recurrence (Table 4).

Hauser et al⁶ reported on 238 people (75% older than 19 years of age) who had a single, nonsymptomatic seizure. Of these 238 individuals, 27% experienced a recurrence by 36 months of follow-up. Approximately one fourth of the patients had had some remote neurologic insult to which the seizure was attributed, and those patients had a higher recurrence rate (31%) than those in whom no etiology could be determined and for whom the recurrence rate was only 20%. EEGs were obtained in almost all patients and were only helpful in predicting recurrence in the small group (5%) with spike-wave abnormalities. In this group, the recur-

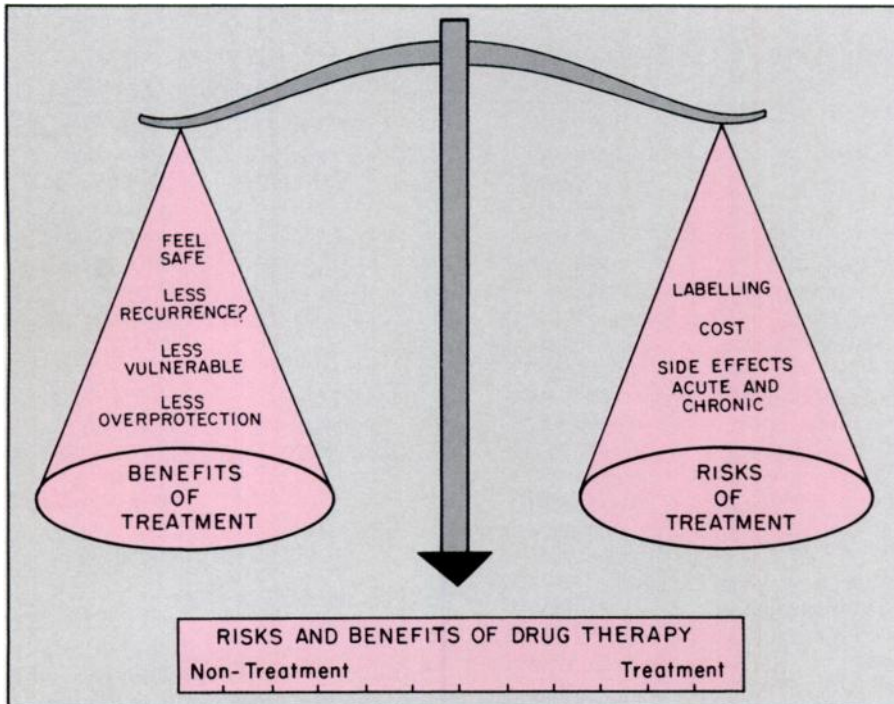


Figure. Balancing risks and benefits of treatment.

rence rate was 50%. There were no EEG data to compare abnormal focal findings. When a sibling had seizures (7%), the recurrence rate was 35%. Abnormal neurologic examination findings were not associated with a significantly increased recurrence risk.

Treatment with anticonvulsant drugs did *not* affect the recurrence rate. Treatment was recommended in 69% of patients, but the choice of drugs and compliance are unknown. One could certainly question whether those with known previous neurologic insult (remote symptomatic) were more concerned about the development of seizures because they knew they had a potential cause and were, therefore, more prone to have medications prescribed and to comply.

The study by Hirtz et al⁷ used the data from the National Collaborative Perinatal Project (NCP) in which approximately 54,000 children were followed from birth to 7 years of age. They reviewed the records obtained at the routine follow-up visits, which were a year apart after 2 years of age. There were 518 children identified as having one or more nonfebrile seizures. One or more recurrences were experienced by 313 (61%). In the group of 435 who did not have

absence, myoclonic seizures, or infantile spasms, the recurrence rate was 55%. Unfortunately, 6% of these children had atypical staring spells, many of which may have been the frequently recurring absence seizures. It is difficult to compare this group to that of Hauser et al but, as in the work of Hauser et al, there is the sense that those with generalized motor seizures (tonic-clonic) had fewer recurrences (48%). No EEG data are available and a significant percentage (27%) may have been treated.

In the most recent study, by Camfield et al,⁸ children were identified from EEG records. Of children with a first seizure, 86% were scheduled to be studied by EEG. Of 757 possible patients, 176 had experienced a single, unprovoked seizure before the EEG and 168 were available for follow-up. More than one seizure was experienced before the EEG by 141 patients, suggesting that somewhat less than 86% of children actually have an EEG performed after the first seizure. There were 428 children who were believed not to have experienced a seizure at all but were believed to have had pallid syncope or breath-holding spells. Unlike the study by Hirtz et al, there were no children with symptomatic seizures.

Seizures were considered focal if there were focal EEG changes, even if only tonic-clonic symptoms were reported. Children were believed to have abnormal neurologic examination findings if there were excessive soft signs. Unlike the studies by Hauser et al and Hirtz et al, children with abnormal neurologic examination findings were believed to have more frequent recurrences; ie, 73%. Therapy was recommended for 70% of the children; compliance was not ascertained.

Camfield et al have generated prognostic data by combining prognostic factors. The best prognosis existed if there were normal neurologic examination findings, a nonepileptiform EEG tracing, and a generalized tonic-clonic seizure. In this population, only 30% recurrence is expected. On the other hand, a child with a partial complex seizure, focal epileptic EEG change, and abnormal neurologic examination findings experienced a 96% recurrence rate.

A fourth study in progress suggests that, in a less biased, prospective population, the risk of recurrence after a first seizure is less than 20%.^{8a}

One constant theme that runs through these three studies is that, if there is a second seizure, the likelihood of a third is 50% to 75%, regardless of other factors. In all three studies, it is clear that, if recurrence takes place, it tends to be within the first 6 months to 1 year after the initial seizure and that recurrence virtually never occurs beyond 2 to 3 years.

Because the generalized tonic-clonic seizure has a reasonably low chance of recurrence (20% to 48%), and because of the consequences of medications, we do *not* usually initiate therapy after a single seizure.

Is medication mandatory after a second seizure? Decisions about embarking on therapy after a second generalized tonic-clonic seizure should include consideration of the time span between the two seizures, the age of the child, and the potential consequences should another seizure occur. Because these consequences may be different, and perhaps less for the younger child as compared with the older child or the adolescent, one cannot make a fixed rule about who should be treated.

TABLE 4. Recurrence After First Nonfebrile Seizure

Study	Age (% of Patients)	Duration of Follow-Up	% Recurring	Favorable Predictors		Unfavorable Predictors		Neutral
				Category (% of Patients)	% Recurring	Category (% of Patients)	% Recurring	
Hauser et al ⁶ (N = 238)	<19 yr (27%)	22 mo	27 (36 mo)	Idiopathic (73) Generalized tonic-clonic (45) Complex partial (7) Simple partial (20)	20	Remote symptomatic (27) Idiopathic & spike-wave (5) Idiopathic & sibling with seizures (7)	31 50 35	Age at first seizure Sex Seizure types Onset with status Idiopathic Abnormal neurologic examination findings Treatment
Hirtz et al ⁷ (N = 435)	1 mo–7 yr	Until 7 yr	55	Generalized motor (72) Symptomatic (3)	48 23	Focal motor (21) Atypical staring (6) Unprovoked (70) Previous febrile seizure (7) Prior neonatal seizure (7)	65 93 69 65 74	Age at first seizure Abnormal neurologic examination findings Family history of non-febrile seizure
Camfield et al ⁸ (N = 168)	1 mo–16 yr	31.4 ± 16 mo	52	Normal neurologic examination findings (82) Tonic-clonic (45)	47 44	Abnormal neurologic examination findings (18) Partial complex (19) Focal epileptic discharge (30) Focal seizure without 2° generalization (20) All focal with 2° generalization (50)	73 79 68 75 60	History of febrile seizure (17) Spike-wave EEG (14)

Certainly, a child who has had two or more generalized tonic-clonic (grand mal) seizures should be considered for therapy. The risks accompanying recurrent seizures and the benefits of therapy should be fully discussed with the family. The risks of use of anticonvulsant agents include both allergic and idiosyncratic reactions, chronic side effects on many organ systems, and the effects on the developing brain. Children with seizures that impair consciousness, such as absence and partial complex seizures, should probably be treated because these types tend to recur frequently, and there may be many subclinical electrical events that can interfere with learning and behavior.

WHY DO YOU TREAT SEIZURES?

Most seizures are treated primarily because of their psychosocial risks, and these risks are clearly age dependent. Although there is a somewhat increased mortality associated with seizures, it is not clear that this is less in patients who are on medication. The risks of status epilepticus

occurring are small, and there are no data to suggest that they are substantially lessened by anticonvulsant medication.^{8b} The effectiveness of anticonvulsant drugs in preventing the recurrence of seizures has also been questioned.⁹ Apparently, prevention of recurrence does not take as smooth and easy a course as we had once thought. Parents need to be aware that medication and dosage must be tailored on an individual basis and that a quick remedy is not always possible.

WHAT ANTICONVULSANT AGENT TO CHOOSE?

For patients with generalized tonic-clonic seizures and simple partial seizures, the standard anticonvulsant drugs are phenobarbital, phenytoin, and carbamazepine. Phenobarbital has been used for generations. It is the cheapest and one of the safest anticonvulsants available. There are rare allergic or idiosyncratic side effects. The major disadvantage of phenobarbital is a 30% to 40% incidence of hyperactivity, behavioral disorders, and sleep disorders in

younger children. Sedation, although usually tolerated, is common, and its effects are often not fully recognized until the medication is discontinued. A recent study indicates that phenobarbital may interfere with learning and behavior even in the absence of observable side effects.¹⁰ For these reasons, it is rarely our first choice drug except when cost or single daily dosing becomes a significant consideration.

Phenytoin is slightly more expensive but also effective. In addition to drug rashes and occasional liver or hematologic side effects, its major unpleasant side effects are gum hyperplasia, occurring in as many as 90% of children, hirsutism, and coarsening of features. Gum hyperplasia may be diminished by good dental hygiene, but there may be major effects on permanent dentition. Because of these side effects, we prefer not to use phenytoin for our initial drug. If phenytoin is used, it should be recognized that generic forms of phenytoin are as effective in controlling seizures as Dilantin, but these generic forms have different rates of absorption and bioavailability. There-

fore, care must be taken to assure similar blood levels when switching from Dilantin to generic phenytoin or when switching between generic phenytoin preparations. The generic form should be used twice a day, whereas Dilantin may be used once a day, except in small children.

Carbamazepine (Tegretol) is said to cause hematologic problems and a host of other side effects. Although the Physicians' Desk Reference (PDR) recommends checking the drug frequently for multiple hematologic and hepatic parameters, the frequency of problems is small and not dissimilar to those found with other anticonvulsant drugs. Although occasional allergic and idiosyncratic reactions may occur, the major dose-related side effects are blurred vision or double vision occurring about 1 hour after a dose. Because the half-life of the drug is short, it is recommended that it be given three or four times a day but we have found that twice daily dosing is usually adequate and tolerated. It would appear that there is less effect of carbamazepine on neuropsychologic function. We prefer it as our initial anticonvulsant medication for most partial seizures and for generalized tonic-clonic seizures.

Sodium valproate (Depakene, Depakote) is a useful drug for patients with tonic-clonic seizures and may be helpful in patients with partial complex seizures. The side effect of most concern is severe hepatotoxicity. This occurs more frequently in the very young child receiving more than one medicine. The most frequently described side effects are gastrointestinal disturbances (alleviated by the enteric coated preparation), tremor, and alopecia. Behavioral and cognitive disturbances appear to be infrequent and generally mild. Half-life is generally believed to be less than

12 hours, but twice daily dosing is usually appropriate. It is our drug of choice for patients with atypical absence, myoclonic and atonic seizures.

MONITORING

The scope of this paper pertains to the more immediate situations of diagnosis, evaluation, and initiation of therapy. It would be remiss, however, not to mention the excellent prognosis for most children. This message should be conveyed to parents and to the children themselves. If seizures can be controlled for 2 years, 75% of children can be slowly weaned from the medication without experiencing recurrence. The decision to withdraw therapy is just as important as the decision to prescribe it.¹¹

While the child is on anticonvulsant drugs, it is important to monitor the child for medication side effects and learning and behavioral problems and to be sure that overprotection and psychologic and social problems are not occurring. Monitoring serum levels of the medication can be useful but serves only as a guide. A medication is efficacious when seizures are controlled without toxicity to the patient; a drug is toxic when the patient experiences side effects. Toxicity does not exist solely on the basis of a reported drug level. It must be correlated with the patient's condition.¹²

SUMMARY

Single, nonfebrile seizures are *not* epilepsy, and although they often cause a major psychic trauma to the family they do *not* necessarily require hospitalization, CT scanning, or extensive workup. Anticonvulsant treatment is *not* obligatory and should, if used, be individualized. Only 30% of

tonic-clonic seizures will recur, and most children who do require therapy can have it discontinued after 2 years.

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