EVALUATION OF THE CHILD WITH THE FIRST SEIZURE

MARVIN A. FISHMAN, MD
This morning I am going to talk to you about the evaluation of the child with the first seizure. And what I hope to do is to point out to you that there's a difference between seizures and epilepsy, that the evaluation is not the same for every child with the first seizure, and in helping plan your approach, one needs to recognize there are factors which will predict seizure recurrence, and that may determine whether you will institute anti-epileptic drug therapy. And if you choose to do so, we want to understand the rationale for doing it, and what you hope to accomplish by your treatment plan.
Now a seizure is not synonymous with epilepsy. A seizure is a clinical manifestation of an abnormal and excessive excitation of a population of cortical neurons. And where those neurons are located, and where the seizure discharge propagates, determines the clinical form that you see. Seizures which in the temporal lobe may be accompanied by déjà vu and other types of autonomic disabilities. Those that occur in the frontal area may involve speech and may involve thought processes. Those in the occipital lobe may have visual symptoms. And then if the discharge starts locally and spreads, then you have your secondary generalized seizure. There are some seizures in which the discharges start in all parts of the brain simultaneously those that we call generalized epilepsies. An example of that would be an absence seizure. But a seizure, as I've pointed out, does not mean epilepsy. Epilepsy is a tendency towards recurrent seizures unprovoked by systemic or neurologic insults. A seizure secondary to hypoglycemia is not epilepsy. The seizure associated with hyponatremia or fever, those are not epilepsies. A seizure that occurs at impact with head trauma is not epilepsy. So there is a distinction.
Epilepsy by nature is a chronic disorder. It means that it recurs and will consistently be followed by additional seizures after the first seizure. Epilepsy is not a single disorder. It’s a whole host of problems with many different etiologies. The prognosis is vastly different for the type of epilepsy that the child may have. There is no one clinical trait in all forms of epilepsy. You can’t say that you can consistently find something in every form of epilepsy. Obviously they have seizures, but the form of the seizures and the other manifestations, they are not consistent in every type of problem. The one thing, though, there are recurrent seizures. And that is the definition of epilepsy. It’s seizures that recur. Or possibly, one might say that there’s one seizure that after it occurs will invariably lead to recurrent seizures. If you have a seizure related to a neuronal migration disorder, or to a benign tumor, if those are not treated, you can well rest assured that there will be recurrent seizures and the development of epilepsy. Now when you’re dealing with the first seizure, there’s no pattern of behavior or movement that is definite proof of seizure activity. And sometimes they can be confusing. You can have convulsive activity that is not necessarily a seizure, and that will come up in just a second.
Epidemiology

Number of people with epilepsy:

• In the United States:
  at least 1 out of every 200 people

• Estimates range from 0.5% to 2% of
  U.S. population

Now how much of an impact is epilepsy? Well, it’s estimated that at least a half percent, or one out of every 200 people in the United States, has epilepsy. And that’s a minimum estimate. The ranges would go up to 2%. And in epidemiologic studies, it has been shown that approximately 6% of children by the age of 5 or 6 will have had a seizure. Not epilepsy. But at least will have a seizure. And the vast majority of those, of course, are febrile seizures.
Questions Raised by a First Seizure

- Seizure or not?
- Focal onset?
- Evidence of CNS dysfunction?
- Metabolic precipitant?
- Seizure type? Syndrome type?
- Studies?
- Start AED?

When you see the first event, the question arises, is it a seizure or not? And as I indicated, and I’ll show you in the next slide, that you may have convulsive activity that is not associated with a seizure. You want to know, did the seizure have focal onset? It’s very unusual that any of us get to witness a seizure. Most of the time you’re going on the history that’s provided by the parent or caretaker. Almost invariably you’ll hear the description, “It’s a generalized seizure.” Because often when the seizure is observed by the parent, it probably is secondary generalized. So it’s important if you can tease out exactly how the seizure began to know whether it had focal onset. And in some children who can recall the event, they may be able to give you a clue as to what they first felt when the seizure started. So you want to try and get that history. Is there other evidence of neurologic disability? Is the child developmentally slow? Does the child have a hemiparesis? That would lead you more toward a high suspicion that you’re going to have recurrent problems. Was there a metabolic precipitant? Did this seizure occur in the face of nausea and vomiting? Could there possibly have been hyponatremia, or hypoglycemia? Those are not going to lead to epilepsy. And then I indicated about the seizure type, and whether its onset was characterized by focal features. Once you get into recurrent seizures, now we not only talk about the seizure type, was it a complex partial seizure, a simple partial seizure, a generalized seizure? We also talk about the epileptic syndrome because that is important in terms of prognosis. One of the most common epileptic syndromes is something called benign rolandic epilepsy. It’s a seizure that usually occurs in sleep, consisting of a partial seizure with difficulty talking, and may have focal clonic activity. Why is that important? That is a benign epilepsy that’s going to remit. That is important information to share with the family. There’s another type of epilepsy syndrome called the juvenile myoclonic epilepsy. It often occurs between five and ten years of age, characterized by a few myoclonic jerks upon awakening. Often you’ll get a history of dropping dishes at breakfast time. It may have generalized seizures as part of it, occasionally absence seizures. Why is that important? It’s easy to treat, and it usually responds well to medication, but it doesn’t remit. And it’s often a lifelong problem. These are important things to have for prognostic discussions with the family. Then after you see this – or have the first seizure, what studies should you order? There is not one shoe that fits everybody. Not every child with a seizure needs every available diagnostic procedure. And then lastly, should you start anti-epileptic drugs? What I’m going to do, hopefully, is give you some information on which to base your decisions.
Evaluation of Children with First Seizures

History
- non-epileptic paroxysmal behavior
- non-epileptic seizure
  - syncope
  - breathholding
  - cardiac origin

Examination - skin, eye, cranium
Laboratory

Now what about that first seizure? As I indicated, there are non-epileptic paroxysmal behaviors. Syncope can be confused with a seizure because in some children who have syncope, they could have convulsive movement and occasionally even incontinence. But usually you can get the history of pre-syncopal symptoms, and then going on to syncope, and the circumstances under which it occurred often give you a clue. Breath holding often is accompanied by convulsive activity. But again, those episodes are always provoked, and when you dig in the history, you can get that information. Long QT syndrome can cause loss of consciousness and occasionally convulsive activity. So the history is important to try and make sure you're really dealing with a seizure that might be cerebral or possible epileptic in origin, as opposed to a convulsive event that is not cerebral in origin. And then of course the examination of the skin, looking for neurocutaneous abnormalities. The eye. Head size is important. Then you have to make the decision of what type of laboratory tests should I do?
Laboratory Tests

- Routine chemistries
- Hepatic and renal function
- Inherited metabolic diseases
- Infectious diseases
- Chromosomes
- Lysosomal enzymes
- Mitochondrial disorders
- Peroxisomal disorders
- Cerebrospinal fluid evaluations

These are the type of things that are available to you. Should they be done on every child? Clearly not, the examination has to be tailored for the circumstances. What about routine chemistries like, electrolytes, calcium, phosphorus, magnesium? They are rarely helpful. I think unless there is a strong indication that there is a situation which might anticipate a metabolic abnormality, vomiting, diarrhea, poor intake, probably these tests are not worth doing. I must say, though, in a newborn we’re a little bit more generous in our application of diagnostic tests and would probably do a more complete battery than an otherwise well child who has a seizure at age three. While I’m thinking about it, in febrile seizures is there any value in obtaining routine chemistries? The answer is no. Absolutely not, unless you have a high index of suspicion that the accompanying illness could lead to a metabolic derangement. You may want to do liver and kidney tests as you start therapy and follow the side effects of some of the anti-epileptic drugs. The other type of disorders, I think you have to have a clinical clue before going after metabolic disorders, infectious disease, chromosomes. You certainly won’t do any of these tests in an otherwise normal child who has a normal neurologic examination and had a seizure. What about CSF evaluations? Obviously, if you suspect an infectious process, then meningitis, encephalitis, of course. Probably in the newborn I would do a CSF examination because there are certain conditions in which you may only diagnose by examining the CSF. There’s one that’s been recently described in which there’s a transport defect of glucose into the brain. It’s called the glucose transporter defect. Serum glucose is absolutely normal. The CSF glucose is low. And it can present with seizures. You would never diagnose it unless you measured the CSF glucose. So in newborns and young infants, I would have a higher index of suspicion and would probably do a CSF examination almost routinely.
Then whether the child is developmentally normal and neurologically normal, when we talk about the other types of seizures, what is your evaluation for these types of seizures? As I indicated for neonatal seizures, although some are benign, it may be very difficult to tell at the onset which way you’re heading. For a neonate, I would tend to do a more exhaustive evaluation, including routine chemistries, CSF examination, and even possibly looking for inborn errors of metabolism such as amino acid and organic acid disorders. In febrile seizures, probably do very little. In an otherwise normal child, who has normal development and has a febrile seizure, I personally would not even do an EEG or any chemistries unless there is a specific indication other than just the fact that there was a febrile seizure. If there is a focal component, many of those children are not going to have anything, but that may trigger an imaging study. But short of that, I don’t think an EEG is part of the routine evaluation of a seizure. Infantile spasms, a lot of the etiology is full evaluation. Post-traumatic epilepsy, probably pretty straightforward, other than imaging and the EEG, don’t need a whole lot. Generalized seizures in terms of a familial idiopathic disorder, again, one does not need a lot of laboratory evaluation. Absence, don’t need anything other than the EEG. Now in myoclonic, minor motor seizures, often associated with a host of neurologic problems and degenerative diseases, a more full evaluation. And the child with a partial seizure probably deserves imaging and an EEG. So I would try and tailor the diagnostic investigation to the status of the child and the type of seizure.
Now what about the EEG? Ictal recording, meaning a recording at the time of seizure, would be wonderful, but that’s not usually what happens. Often you’re ordering the EEG after the seizure. So then you’re left with the interictal recording. This can be helpful looking for a focus or a susceptibility to seizures, but it doesn’t diagnose epilepsy. Children who have seizures can have a perfectly normal interictal EEG. The EEG is helpful in monitoring situations. If you have recurrent episodes that you’re not sure whether these are seizures or some other type of behavioral manifestation, if they’re occurring frequently enough that you can capture an event and do a simultaneous video EEG monitoring procedure, then that would be helpful. Occasionally you can’t tell whether the seizure may be arising from the temporal lobe. Is it a secondary generalized seizure or a primary generalized seizure? The EEG may be helpful. In terms of looking for pseudoseizures, in other words nonepileptic seizures, the EEG would be helpful particularly if you can capture a clinical event. And in terms of assessing therapy, the one situation in which the EEG is helpful is an absence epilepsy. That is one epilepsy in which successful treatment will reverse the EEG abnormality, so you may use it for that. In other types of epilepsies, the clinical response is what you would follow, not necessarily the EEG and you would not anticipate reversing an abnormal EEG other than an absence.
• Normal EEG does not rule out epilepsy

• Minor abnormalities frequently occur and do not confirm the diagnosis of epilepsy

So the normal EEG does not rule out epilepsy. Many children will have minor abnormalities which are found, and in as much as 30% of the population, there are some slow waves, occasional sharp waves, which they do not confirm the diagnosis of epilepsy. For the most part it's still a clinical diagnosis.
Now let's talk about neuroimaging, which is the next major procedure. What is the purpose of doing an imaging study? You want to see if there's a structural lesion that requires surgery, and identify a brain abnormality such as a migrational disorder, a porencephalic cyst that might be the cause of seizures. Epileptologists who are planning surgery are going to do imaging to see if there's a correlate to the EEG. And sometimes you get a better understanding of the epilepsy by doing an imaging study.
Which imaging study should you do, the CT or MRI? Generally the MRI is the most sensitive test and is now the procedure of choice in evaluating a child with epilepsy. Often the CT will be done in the emergency center and for a screening type of event. At this time I would think that is not a complete diagnostic evaluation. Particularly if you are dealing with someone with a partial seizure, you'll need to follow that up with an MRI. Will it affect your therapy? Possibly. You may find a small tumor that was not apparent on CT, and you may get a better understanding of the etiology of the epilepsy by finding a migrational disorder.
And just to give you an example of that, there was a study done – and this is a particular situation in which patients were having temporal lobe surgery for treatment of their epilepsy – and these patients had both a CT and an MRI. And then they had surgery. So the gold standard was the brain tissue itself, removed at the time of surgery.
And what did it show? The MRI was abnormal in 70% of the situations, and the CT in less than 20%. Looking for a mass lesion – these were small tumors, benign, 100% on MRI, but only 2/3 of the CTs picked up the change. When you’re looking for gliosis or scarring that often goes along with temporal lobe epilepsy, you’re not going to see it on CT, only on MRI. So this is just one example of how much more utilitarian the MRI is compared to the CT.
Then after you’ve dealt with the first seizure and planned your diagnostic investigations, what do you do then? Do you start treatment? One of the things that you should consider is, what is the recurrence risk after the first seizure? Various studies will indicate anywhere from a 30 to a 60% chance. As you can see, it’s all over the ballpark. And in some situations I’ll show you, it’s even higher than 60%.
Factors Affecting Recurrence Risk

EEG - Increased risk with
- abnormal interictal record
- generalized spike-wave pattern
- focal spikes
- focal or generalized slowing

An abnormal EEG does increase your risk for recurrence. If you have an abnormal interictal record with spike discharges and epileptogenic foci, that child is more likely to have a recurrence. If you have a generalized spike wave pattern, again you’re more likely to have a recurrence.
Let’s look at that data. Here I am referring to idiopathic in which there is no apparent cause. And then if you take a normal EEG versus an abnormal EEG – and this is all types of seizures – you see that the recurrence risk is almost doubled if you have an abnormal EEG. So that may help in your assessment as to whether the child needs to be treated. The EEG will give you prognostic information regarding recurrence.
Factors Affecting Recurrence Risk
Seizure Classification

- Risk greater after partial seizure compared to generalized seizure
- Partial seizures more common in children with remote symptomatic first seizure (80%) with idiopathic seizure and abnormal EEG
- Children with idiopathic first partial seizure and normal EEG may have similar risk to those with generalized seizure

The risk is much greater after a partial seizure than a primary generalized seizure, if you have a child with a complex partial seizure or a focal seizure, because usually those reflect remote insults. And they often reflect abnormalities that you may see on the MRI. If you have a child who has an idiopathic seizure, but an abnormal EEG, the recurrence risk is going to be higher. So the basic thing is that partial seizures have a much higher chance for recurrence, and a partial seizure with an abnormal EEG has even a higher risk of recurrence.
Risk of Recurrence of Non-Febrile Seizure

- Absence, Akinetic, Myoclonic, Minor Motor: 100%
- Infantile Spasm: 100%
- Partial Complex: 80 - 90%
- Focal Motor: 65%
- Generalized Tonic-Clonic: 45%

Now that first slide said 27 to 62% of children have recurrences. You have to know how this study was done and what type of seizures were eliminated in their consideration. If you see a child with an absence seizure, you can bet your bottom dollar there’s going to be more absence seizures. That’s 100%. Usually by the time you see them, there’s not only one, they’ve already had many. Same thing with infantile spasms. You see one spasm, you know for sure there’s going to be a recurrence. You don’t have to wait around in those circumstances. Again, with partial seizures, and particularly a partial complex seizure, the risk of recurrence is going to be 80 or 90%. With just a focal seizure, without impairment of awareness, it’s about 2/3. If you take a child with a generalized tonic-clonic seizure, no etiology, otherwise normal, that risk for recurrence is going to be 50% or less. So the recurrence risk is not the same, and that will influence your thinking about whether you should start anti-epileptic drug therapy. If there is going to be a recurrence, when is it going to happen? Again, we talked about remote symptomatic, and that almost equates with partial complex seizures, versus no known etiology for the seizure, an idiopathic one.
Factors Affecting Recurrence
Risk After First Seizure

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<th>Remote</th>
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<tr>
<td>12 months</td>
<td>37%</td>
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<td>24 months</td>
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<td>36 months</td>
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You can see that in the remote symptomatic group you’re almost twice as likely to have the seizure. So let’s look – if you have a child who has an idiopathic, single generalized seizure, otherwise well, the chance for recurrence – and say the EEG is all right, also – the chance for recurrence is going to be less than 50%. Would you start treatment when you have as much chance of not having another seizure as you do of having another seizure? And that’s why I think you have to take that into consideration.
Age in most studies is not a factor regarding recurrence. In the National Collaborative Perinatal Project, children less than two years of age with a focal motor seizure tended to have a recurrence. And I must say that with the onset of focal seizures in a teenager, you’re more likely to have recurrence. But otherwise age is not a big factor in predicting recurrence.
Factors Affecting Recurrence Risk
Family History

- Variable effect
- May be important in children with idiopathic first seizure and abnormal EEG

Family history is variable unless you’re dealing with one of the genetic epilepsies. And under those circumstances, a positive family history, obviously, is going to indicate a much high recurrence risk.
The duration of the first seizure. Does that predict recurrence? The answer is no. You are no more likely to have a recurrence risk after an episode of status epilepticus in an otherwise normal child than you are if that seizure lasted two minutes. And if you look at whether it’s a two minute seizure, 15 minute seizure, or a 30 minute seizure, it does not affect the recurrence risk. It affects your thinking. Now obviously this was a dramatic event. The seizure went on for 30 minutes. You’re scared. I’m scared. The parents are scared. But when you get right down to it, it doesn’t affect recurrence. And so pulling the trigger for treatment on the basis of the length of seizure doesn’t really have any justification. And the length of the first idiopathic seizure, if there is going to be a recurrence, does not predict that all the future seizures are going to be long ones either.
Other factors that predict an increased risk for recurrence are neonatal seizures. Teenagers with focal onset are going to have a higher risk of recurrence. Focal epileptic discharges on the EEG increase the risk. And a developmentally or neurologically abnormal child is going to have a greater risk. Again, they predict recurrence, but none of these are 100% factors.
Now if there is going to be a recurrent seizure, when is it going to happen? The vast majority, by a year and almost all by 24 months. So if you decide not to treat, and wait, the parents will often ask, “Well, how long do I have to wait?” Well there’s not a definite answer, you may have to wait a long time. But the vast majority of recurrences are going to occur by a year. So if there is no recurrence by a year, then the likelihood of recurrence becomes less, and you can still relax a little bit more. Now I must say that if I choose not to treat a child after the first seizure, I think you still should counsel the parent about seizure precautions and seizure management. I think that’s important to do. If you decide not to treat, and a child has a prolonged seizure, I think more often now that we are suggesting that the families have Diastat available, which is a rectal diazepam preparation for recurrent seizures. Many families now are comfortable with that. If they know they have something that they can use at home that will be helpful, they often will accept that management or endorse that management form without the need to start anti-epileptic drugs. So what I'm trying to say, you have to individualize your treatment plan, and you can use data such as the type of seizure, the status of the child, and the EEG to help you decide what the recurrence risk is going to be.
Now what are the reasons for treating the first seizure? One, to prevent recurrences. That’s clear. But as I indicated, in some situations it’s more likely than not that the seizure won’t recur. So is recurrence the big factor? Reduce the risk of brain injury? You know, there really is very little data that a seizure in a normal child produces brain injury unless there’s a concomitant factor such as hypoxia, ischemia, or something else. But even a 30-minute seizure most often will not produce brain injury. So the idea of preventing brain injury by treatment, while intuitively it seems to make sense, there is very little data to support that. Will you reduce the risk of developing intractable epilepsy? Again, that’s a dictum that’s been in our heads a long time. Seizures beget seizures. But the data is not very good to support that. So you may not be able to modify the course of whether an epilepsy is going to become retractive or not, whether you treat it or not. It may be a factor of the epileptic syndrome, as I indicated, in terms of whether it’s going to remit or not, and whether you have a situation such as a gliosis, benign tumor, scar. Those epilepsies are less likely to remit.
So, what about the first seizure? Whether to treat or not is controversial. And what I’ve tried to indicate to you, that there is not one answer that’s applicable for all children and all types of seizures. The recurrence rate is going to be very high, and it may be as high as 85% within a couple of years; although some studies, depending upon which type of seizures were included, will indicate the recurrence will be 60% within five years. Drug treatment will reduce recurrence. Is that always necessary? Abnormal imaging and an abnormal EEG, a family history of a genetic epilepsy, increase the recurrence risk. And quality of life issues have to be considered. A teenager that has two or three seizures a year may be much more devastated by that than an infant in a preschool situation that has two or three seizures a year. So I think you have to consider the impact on the patient and how that’s going to affect their function.
So what do you accomplish if you treat with the first seizure? You probably reduce the recurrence risk, but that is not even consistent in all studies. And on some studies, when they are analyzed on intent to treat – in other words, you prescribed a medicine, and you don’t know whether the patient took it or not – real life. If you look at it that way, on some of those studies there hasn’t been a major impact by treating the child. Now in most situations that’s excluding children who have absence epilepsy and others. But if you take away those epileptic syndromes, what you do by prescribing the medication is unclear. In studies in which it has been followed that the drugs have been maintained in a therapeutic range, there clearly is a reduced risk of epilepsy.
Recent Data Suggests

- Many children with single seizure do not have further seizures
- Many children become seizure free
- AEDs may be withdrawn after relatively brief seizure free period
- Prolonged seizures may not cause brain damage unless associated with acute neurologic insult

So in summary then, many children with a single seizure do not have further seizures. Therefore every child who has a seizure does not need to be put on anti-epileptic medications. The evaluation will be based in part upon the age of the child, the other types of disabilities, and the type of the seizure. Many children will not have recurrences, and many children will become seizure-free. If you decide to treat after one or two seizures, should that child have two or three years of anti-epileptic drug therapy, seizure-free? I think not. And many of us now are treating for much shorter periods of seizure-free intervals, anywhere from six to twelve months. And prolonged seizures may not cause brain damage unless there is an associated acute neurologic insult. So while the prolonged seizure is frightening to everyone, it in itself may cause damage, and may not be an indication for continuous anti-epileptic drug therapy. And with that, I'll close and thank you.