



## How to Succeed with Epilepsy Syndrome Diagnosis

The process will shed light on the prognosis, and will help to direct your approach to management.

**E**pilepsy is one of the first recorded neurological disorders, having been alluded to by Hippocrates himself. It is the second most common neurological condition, affecting up to one percent of the population. In the United States and Europe, the annual rate of new cases is estimated at up to 40/100,000.<sup>1</sup> Epilepsy occurs most often in the very young and the elderly.

Neurologists are usually the ones who diagnose and treat seizures. However, the list of epilepsy syndromes continues to grow as more are recognized. In addition, the classification of the epilepsies continues to change. To add to the complexity of the situation, the list of available treatments continues to grow as well. Nowadays medications, the ketogenic diet, devices for seizures and epilepsy surgery are only some of the possible treatment options. As this list of therapies grows, it becomes increasingly difficult to select the most appropriate method. This installment of Epilepsy Essentials will begin to address at least one part of the problem that neurologists face: epilepsy syndrome diagnosis.

### What is an Epilepsy Syndrome? What is its Importance?

Epilepsy is not a single entity. It is a term that encompasses many different kinds of seizure disorders. In order to firmly establish an epilepsy syndrome diagnosis (Table 1), the neurologist must assemble information from the patient's history, neurological examination and the results of medical testing.

The first step in the management of

epilepsy begins with seizure and, more specifically, epilepsy syndrome classification. While there are numerous ways to classify seizures, epilepsy syndrome classification is the most comprehensive. Seizures may be classified on their degree of cerebral involvement as either partial seizures or generalized seizures. Semiological classification based on regional features is also useful, specifically when focusing on localization. However, differentiating events based on their clinical pattern alone provides only a fraction of the picture. To most accurately determine the natural course of a seizure disorder and to identify the most promising treatment option, classification based on epilepsy syndrome is the strongest tool available.

But how do we go from meeting a person with epilepsy to establishing an epilepsy syndrome diagnosis? The International League Against Epilepsy (ILAE)<sup>2</sup> has developed a five-step process to help (Table 2). The first step, ictal phenomenology, is to identify the characteristics of the patient's event(s). Step two, the neurologist must use this information to identify the seizure type. Third, the seizure information along with other historical information is combined to formulate an epilepsy syndrome diagnosis.

Once this is done, the neurologist is now better equipped to look for specific causes. For instance, a person with complex partial seizures that arise from the temporal lobe may have mesial temporal sclerosis. By identifying the syndrome first, the physician is less likely to miss this as a possible etiology of the person's seizures. Finally, the epilepsy syndrome

diagnosis can also be used to establish a prognosis (Figure 1). For instance, some syndromes spontaneously remit while others would be expected to be lifelong.

### Steps 1, 2 and 3: Phenomenology, Seizure Type, Epilepsy Syndrome

When a person seeks medical attention for episodes of recurrent neurologic dysfunction, a broad differential diagnosis must be considered. Paroxysmal movement disorders and sleep disorders are often mistaken for seizures. Transient alterations in cerebral blood flow and oxygenation, such as those that occur during a TIA, orthostasis or migraine, may cause recurrent events that resemble epilepsy. However, epilepsy is characterized by recurrent, highly stereotyped episodes of neurological dysfunction.<sup>3</sup>

When considering the diagnosis of epilepsy, the neurologist should assemble a list of possible risk factors (Table 3). The family history may identify affected first-degree relatives. A genetic link would suggest one of the idiopathic epilepsies. A history of cerebral injury (head trauma, infection, stroke) would strongly support one of the partial (localization related) epilepsies. A combination of developmental delay and multiple seizure types would indicate a possible diagnosis of symptomatic generalized epilepsy.

A careful and thorough history of the patient's seizures is an initial step toward determining the seizure type (Table 4). Seizures often affect a person's thinking and memory. A historical account from friends and family members is needed. The history must include a description of

**Table 1. A Very Broad Classification of Epilepsy Syndromes**

**Idiopathic Generalized:**

- Childhood Absence Epilepsy
- Juvenile Absence Epilepsy
- Juvenile Myoclonic Epilepsy
- GTCs on awakening

**Symptomatic Generalized:**

- West Syndrome, also called Infantile Spasms
- Lennox-Gastaut

**Idiopathic Localization Related:**

- Benign Rolandic Epilepsy, also called Benign Epilepsy with Centrotemporal Spikes (BRECTs)

**Symptomatic Localization Related:**

- Temporal Lobe Epilepsy
- Frontal Lobe Epilepsy
- Parietal Lobe Epilepsy
- Occipital Lobe Epilepsy

**Table 2. ILAE Approach to the Epilepsy Syndromes**

Step 1: Ictal phenomenology  
(description of clinical events)

Step 2: Seizure type  
(partial versus generalized seizures)

Step 3: Epilepsy Syndrome  
(idiopathic versus symptomatic)

Step 4: Etiology

Step 5: Prognosis

all of the patient's events. It is not uncommon for a person with a single type of epilepsy to experience more than one kind of seizure. For instance, a person with temporal lobe epilepsy may experience simple partial seizures, complex partial seizures, and seizures that are secondarily generalized.

Partial epilepsies begin in a focal region of cerebral cortex, and may be *simple* or *complex*. In a simple partial seizure the person retains awareness, and is able to explain the experience. If the seizure affects level of consciousness it is termed a complex partial seizure. However, the seizure can spread or travel through connections to nearby neurons, propagation may even travel to the opposite hemisphere through interconnections in the corpus callosum. When the seizure spreads to involve enough cerebral cortex, consciousness can no longer be maintained. At this point, we call the seizure *secondarily generalized*. Typically, it starts with a tonic phase followed by a clonic phase; in other words, it is a tonic-clonic seizure.

The *initial* clinical and physical manifestations of a partial seizure depend on where the seizure starts. For instance, a

simple partial seizure that occurs in the occipital lobe produces visual hallucinations such as sparkling lights (usually in one visual field). A simple partial seizure which starts in the parietal lobe may manifest as unilateral arm or leg clonic movements. If the seizure starts in the frontal eye field (frontal lobe), contralateral eye deviation occurs.

Generalized seizures manifest in different ways. In a generalized seizure, nearly all of the cerebral cortex is involved from the onset of the seizure. In other words, there can be no "aura." The person cannot retain awareness of the event because consciousness is lost immediately.

There are several kinds of generalized seizures. Absence seizure appears as unresponsive staring, typically lasting 30 seconds or less. Cognition is interrupted, but the person may immediately resume the activity that they were performing at the time that seizure started. In short, it is almost like the person was briefly "put on pause." Because they are so brief, an observer might easily confuse this type of seizure with "daydreaming."

Myoclonic seizures are very brief. Most people describe them as "split-sec-

ond." They consist of bilateral jerking of the arms and/or legs. If the person is holding a toothbrush when this occurs, they might drop the brush or "fling it" from their hand. Because these are so brief, the person who experiences them is usually not aware of an interruption in consciousness. A good example of this is sneezing. The sneeze itself is so brief that it would be impossible to say whether or not there was loss of consciousness during the event. When testing has been done during myoclonic seizures, a sub-second period of altered awareness can be shown to occur.

Generalized tonic-clonic seizures can be generalized at onset. They are clinically identical to seizures that start in a focal region of brain *once the partial seizure has become secondarily generalized*. There is an initial tonic phase (the stiffening) followed by clonic movements of both arms and legs. The clonic movements start out as low amplitude and fast. As the seizure progresses, the clonic movements slow in frequency, but increase in amplitude. As the seizure stops, the person almost seems to "relax." When the clonic activity ends, breathing returns to normal. If the person has become cyanotic, he will quickly return to normal color at this point.

Other, less commonly occurring generalized seizure types are clonic, tonic and atonic. These occur most often in people who have some sort of intellectual disability, usually due to diffuse or multifocal brain injury. All three seizure types are brief, lasting less than 30 seconds. Tonic seizures consist of stiffening only. Atonic seizures consist of a sudden loss of tone. Clonic seizures manifest as bilateral rhythmic arm and leg movements. Though short, these seizure types are the most injury-causing. For instance, a person with atonic seizures who suddenly loses tone will fall. This can result in broken bones, burns or serious head injuries. Children and adults who have this type of seizure may need to wear a protective helmet to prevent at least some of the more serious injuries.



# EPILEPSY ESSENTIALS

By Steven Karceski, MD and Nishi Rampal, MD

## Step 4: What is the Cause?

In the field of epileptology, *idiopathic* does not mean *unknown*. Because many of these syndromes have now been identified as familial or genetic in origin, *idiopathic* is often used interchangeably with *genetic*. There are both genetic localization related seizures and genetic generalized seizures. One example of this is Benign Epilepsy with Centrotemporal Spikes, which used to be called Benign Rolandic Epilepsy. In this syndrome, which is genetic, the onset of seizures occurs in childhood. The EEG shows epileptiform discharges in the region of the Rolandic fissure (also called the central sulcus). These have a characteristic morphology, and tend to markedly increase in frequency during sleep. The combination of partial seizures, a positive family history, and the characteristic abnormality on EEG, the diagnosis is almost certain. Treatment is effective at low doses (when needed). However, most children will “grow out” of this kind of epilepsy by the time of puberty. In other words, the prognosis is excellent.

In contrast to the idiopathic epilepsy syndromes, symptomatic epilepsies can have many different causes. Basically, any process that can cause a focal cerebral injury can cause focal seizures. If a person came to the office describing episodes that began with déjà vu or an unpleasant smell, the neurologist might consider seizures that arise from the temporal lobe. A history of a significant head injury, which is most likely to affect the temporal lobes, would support this. In this case, the person would be labeled as having symptomatic localization related epilepsy. An MRI, directed at carefully evaluating the temporal lobes, would be indicated.

## Table 3. Risk Factors for Epilepsy

- Perinatal insult
- Abnormal gestation or delivery
- Febrile convulsion
- Developmental delay
- Family history of epilepsy
- CNS infection
- CNS mass lesion
- Head injury (with loss of consciousness for > 30 minutes)
- Stroke (ischemic or hemorrhagic)

## Table 4. Seizure Types

### Seizures with partial onset:

- Simple partial seizures
- Complex Partial seizures
- Secondarily generalized tonic-clonic seizures

### Seizures with generalized onset:

- Absence seizures (typical and atypical)
- Myoclonic seizures
- Tonic seizures
- Clonic seizures
- Atonic seizures
- Generalized tonic-clonic seizures

Symptomatic generalized epilepsy is the most difficult to understand. In fact, there is controversy over whether or not this should be used as a category at all. In this group, multifocal or diffuse brain injury has occurred, often early in life (or *in utero*). One example of this would be tuberous sclerosis. In this group of epilepsy syndromes, almost any kind of seizure, or combination of seizures (both partial and generalized), is possible.

## Step 5: Prognosis

Understanding the epilepsy syndrome can help the neurologist to establish a prognosis. Is this a kind of epilepsy that is likely to remit? How likely is this form of epilepsy to respond to medications? Are high doses of medicines likely, or will the seizures respond to low doses? Is the patient going to need epilepsy surgery? The answers to these questions are helpful not only to the doctor but also in

addressing the patient’s and their family’s expectations.

In general, the idiopathic epilepsies have the best prognosis. The term “benign” often appears in the names of these syndromes for several reasons. Although seizures in and of themselves are not necessarily “benign,” these syndromes are more likely to remit when they start in childhood. In fact, up to 85 percent of childhood idiopathic epilepsies will remit by adolescence. The idiopathic epilepsies that start in adolescence or adulthood are unlikely to remit; however, they usually respond very well to one medication, often at low doses. As such, side effects occur less frequently. These factors contribute to the idea that idiopathic epilepsy is “benign.”

Symptomatic partial epilepsy has an intermediate prognosis (Figure 1). Some will be controlled very well with one or more antiseizure medications: in general,

## Figure 1: Epilepsy Syndromes and Likely Prognosis

**Idiopathic** Localization Related or **Idiopathic** Generalized Epilepsy Syndromes

**Symptomatic** Localization Related Epilepsy Syndromes

**Symptomatic** Generalized Epilepsy Syndromes

Good

Poor

about two-thirds will experience good seizure control. The remaining third may be labeled as *refractory* or unlikely to respond to medications. In these instances, epilepsy surgery, aimed at removing or interrupting the seizure-causing area, may be performed. Although the most invasive established treatment for epilepsy, brain surgery can have excellent results. Patients who might benefit from this type of treatment must be carefully evaluated.

The group with the worst prognosis are those with symptomatic generalized epilepsy. In general, about 30 percent of people with this kind of epilepsy will have good seizure control. Not only are they more likely to be refractory, but the surgical options are more limited. Corpus callosotomy may help some people with tonic or atonic seizures. However, unlike the partial epilepsies where seizure-freedom is the goal of resective surgery, only

five to 10 percent of people will stop having seizures after corpus callosotomy. In most instances, the best that can be expected is a reduction of seizures.

### Conclusions

The first step to understanding a person's epilepsy is to identify the seizure phenomenology. Next is to determine the type of seizure with the aim of characterizing the epilepsy syndrome. Medical testing may support the diagnosis, and in many cases will identify the underlying cause. Appropriate treatment and the assessment of prognosis are based on correct identification of the epilepsy syndrome. Because there are so many treatments: antiepileptic medications, ketogenic diet, epilepsy surgery and medical devices, it can be difficult to know which treatment (or combination) is most likely to help. An understanding of the epilepsy syndrome is the

clinician's strongest tool. With it, the physician can optimize medical and surgical management, patient expectation, and quality of life. **PN**

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