Epilepsy Overview and Revised Classification of Seizures and Epilepsies

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ABSTRACT

PURPOSE OF REVIEW: The classification of seizures, epilepsies, and epilepsy syndromes creates a framework for clinicians, researchers, and patients and their families. This classification has evolved over the years, and in 2017 the International League Against Epilepsy (ILAE) published an operational classification of seizures and epilepsies. Understanding this classification is important in the diagnosis, treatment, and understanding of seizures and epilepsies, including epilepsy incidence.

RECENT FINDINGS: The 2017 ILAE classification system builds on newly formulated definitions of seizures and epilepsy. Seizure classification begins by determining whether the initial manifestations of the seizure are focal or generalized. If the onset of the seizure is missed or unclear, the seizure is of unknown onset. Focal seizures are classified according to the individual’s level of awareness, the most prominent motor or nonmotor features of the seizure, and whether the focal seizure evolves to a bilateral tonic-clonic seizure. Similarly, generalized seizures are classified according to motor or nonmotor manifestations. Motor seizures are either tonic-clonic or other motor seizures. Nonmotor generalized seizures primarily refer to absence seizures. Similar to seizure classification, the epilepsies can be classified as focal or generalized. In addition, the new classification system recognizes two new categories: combined generalized and focal epilepsy and unknown epilepsy. The concept of an epilepsy syndrome has been introduced under the new classification system and refers to a cluster of features incorporating seizure types, EEG, imaging, and other features including genetics. The new classification system emphasizes the etiology of seizures and epilepsies.

SUMMARY: The recent ILAE seizure and epilepsy classification system aims to create a framework to better classify seizures and the epilepsies. Universal adoption and implementation of this system will enable patients, their families, clinicians, and researchers to better define and treat the epilepsies. Incidence studies have not generally classified seizures and the epilepsies, and use of this classification system, which emphasizes etiology, will lead to a better understanding of epilepsy incidence.
INTRODUCTION

Seizure and epilepsy classification systems have been used in clinical practice and research since the 1970s. Over the years, multiple revisions have been implemented, the most recent of which is the 2017 International League Against Epilepsy (ILAE) operational epilepsy classification system. This system aims to better define seizures and epilepsies by classifying them using key clinical features, EEG findings, imaging, and genetics. This article reviews the history of epilepsy classification and the details of the 2017 system, with an emphasis on the importance of classification in epilepsy incidence studies.

HISTORICAL OVERVIEW OF SEIZURE, EPILEPSY, AND EPILEPSY SYNDROME CLASSIFICATION

Seizure and epilepsy classification has evolved over the years. Prior to the first modern seizure classification by Gastaut in 1969, seizures and epilepsy types were not distinctly recognized. Although initially met with resistance, this system gained international recognition after 1970 and was widely used. In 1981, the ILAE, informed by advances in technology—notably video recording with simultaneous EEG—published a classification of seizures followed by a proposal of epilepsy classification in 1985, which was then revised in 1989, wherein the concept of an epilepsy syndrome was introduced.

The ILAE then began an effort to revise seizure terminology and the organization of seizures and the epilepsies. This effort culminated in the 2017 published ILAE operational classification of seizure types and epilepsies.

The 1981 ILAE seizure classification system dichotomized seizures into either partial or generalized seizures. Partial seizures were defined as an epileptic seizure in which “the first clinical and EEG changes indicate initial activation of a system of neurons limited to part of one cerebral hemisphere.” Partial seizures were subdivided by level of consciousness: simple partial seizures were associated with no impairment of awareness, and complex partial seizures were associated with impairment of awareness. A third partial seizure type included seizures that evolved to a secondary generalized convulsion. A generalized seizure was defined as a seizure “in which the first clinical changes indicate initial involvement of both hemispheres.” Six generalized seizure types were identified: absence, myoclonic, clonic, tonic, tonic-clonic, and atonic.

The 1985 epilepsy classification was also a dichotomized system dividing epilepsies into either idiopathic or symptomatic. The term idiopathic derives from the Greek idios, meaning self, own, and personal. Idiopathic epilepsies and syndromes were described as disorders “not preceded or occasioned by another.” In these disorders, no underlying cause is present other than a possible hereditary predisposition. Notable idiopathic epilepsies included juvenile myoclonic epilepsy and childhood absence epilepsy. Symptomatic epilepsies occurred because of a known disorder or lesion. A revision of the epilepsy classification in 1989 added cryptogenic epilepsies, which were likely symptomatic, but a cause was not identified.

Since the seizure and epilepsy classification systems were developed in the 1980s, many advances in neuroimaging, genetics, and molecular biology have occurred. Although the newly published seizure classification primarily incorporates the signs and symptoms of seizures and EEG findings, the classification of epilepsy type and syndrome encompasses these new advances.
The current classification systems build on newly formulated definitions of seizures and epilepsy. The 2005 updated seizure definition is a “transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.” Further, in 2014 the ILAE redefined epilepsy as a disease and not a disorder to emphasize the importance and impact of epilepsy. Epilepsy occurs when an individual has an epileptic seizure and his or her “brain...demonstrates a pathologic and enduring tendency to have recurrent seizures.”

Previously, epilepsy was diagnosed when an individual had at least two unprovoked or reflex seizures more than 24 hours apart. Reflex seizures are stimulus-sensitive or sensory-evoked seizures. Although the new definition of epilepsy includes this presentation, epilepsy is also diagnosed if a person has one unprovoked or reflex seizure and has a probability of at least 60% of having another seizure within the next 10 years. The probability of at least 60% was chosen for this definition because this is the lower limit of the confidence interval for someone with two unprovoked seizures having another seizure within 10 years.

In addition, epilepsy is diagnosed when an individual has an epilepsy syndrome. An analysis of retrospective cases supports the applicability of this new definition. In patients with a single unprovoked seizure, a second seizure occurred in more than 80%. The definition, however, does not clarify what metrics should be used to identify patients at risk for a recurrent seizure.

Just as multiple scenarios lead to an initial diagnosis of epilepsy, multiple circumstances can contribute to epilepsy being considered resolved. Epilepsy is considered resolved when a patient with an age-dependent epilepsy syndrome is older than the age in which this syndrome was active or when a patient has been seizure free for 10 or more years and has been off all antiepileptic drugs for 5 or more years.

CLASSIFYING SEIZURES, EPILEPSIES, AND EPILEPSY SYNDROMES

The report by the Institute of Medicine, “Epilepsy Across the Spectrum,” emphasizes the heterogeneity of seizures and the epilepsies. Making sense of this heterogeneity requires a system to provide a common language. To classify means to arrange something into classes or categories according to shared qualities or characteristics. The prior and current classification systems aim to group seizures according to clinical presentation and brain region onset and to group epilepsies according to seizure type, age of onset, probability of remission, EEG findings, radiologic findings, and genetics. Classification of seizures, epilepsies, and epilepsy syndromes creates a framework for patients, their families, clinicians, and researchers.

For patients, the universal common language of the classification system provides a name and diagnosis, which improves understanding and recognition of the disease. Moreover, this common language enhances communication between patients, their families, and providers.

Similarly, clinicians can use the language to better communicate with patients and colleagues. The classification systems allow clinicians to consider history and include data from new technologies when making a diagnosis, choosing treatment, and assessing prognosis.

For researchers, these systems enable standardized investigation of seizure and epilepsy presentation, etiologies, and drug or surgical treatments. For example, when studying incidence patterns of epilepsy, using a common
language and classification enables comparison across multiple populations and studies.

**UPDATED SEIZURE CLASSIFICATION**

With the exception of neonatal seizures, the new seizure classification applies to adults and children. The new classification addresses the limitations of the 1981 seizure classification, which include the following: (1) some seizure types can have either focal or generalized onset, (2) lack of knowledge about seizure onset makes a seizure unclassifiable and difficult to place within the 1981 system, (3) retrospective seizure descriptions often do not include the level of consciousness, (4) terms used in the 1981 seizure classification such as complex partial or simple partial are difficult to understand, and (5) some seizure types are not included in the 1981 classification.

To address needs of different clinicians and researchers, both basic (FIGURE 1-1) and expanded (FIGURE 1-2) versions of seizure classification were created. The basic version of the seizure classification is a contracted form of the expanded classification and is intended to be more useful for pediatricians, non-neurologists, general neurologists, physicians in general practice, nurses, and health care workers. The expanded version is more detailed and will likely be used more by epileptologists/neurophysiologists and researchers.

Seizure classification starts with whether the initial manifestations of the seizure are focal or generalized. Focal seizures originate within a neuronal network limited to one hemisphere that may be discretely localized or more widely distributed, whereas generalized seizures originate at some point within the brain and rapidly engage bilateral distributed networks. If the onset of the seizure is missed or is unclear, the seizure is of unknown onset.

Beginning in 2010 the term focal seizure officially replaced partial seizure. The term focal seizure had been used prior to the 1981 classification system, at which time partial seizure had replaced focal because of concern that its use was confusing and inferred onset in a very restricted area of brain (some seizures may involve large parts of a hemisphere). It is, however, now felt that the term focal seizure is more widely understood.

**Focal Seizures**

Focal seizures are classified according to the patient’s level of awareness and the first most prominent motor or nonmotor features of the seizure. These early

![Diagram of seizure classification](https://example.com/diagram.jpg)

*FIGURE 1-1*

Basic version of 2017 International League Against Epilepsy seizure type classification.


**KEY POINTS**

- In 2014 the International League Against Epilepsy redefined epilepsy as a disease and not a disorder to emphasize the importance and impact of epilepsy. Epilepsy occurs when an individual has an epileptic seizure and his or her “brain demonstrates a pathologic and enduring tendency to have recurrent seizures.”

- Prior and current classification systems aim to group seizures according to clinical presentation and brain region onset and epilepsies according to seizure type, age of onset, probability of remission, EEG findings, radiologic findings, and genetics.

- The 2017 International League Against Epilepsy seizure classification addresses limitations of the 1981 seizure classification, which include the following: (1) some seizure types can have either focal or generalized onset, (2) lack of knowledge about seizure onset makes a seizure unclassifiable and difficult to place within the 1981 system, (3) retrospective seizure descriptions often do not include a level of consciousness, (4) terms used in the 1981 seizure classification such as complex partial or simple partial are difficult to understand, and (5) some seizure types are not included in the 1981 classification.
prominent features are important to consider when localizing the seizure onset or epileptogenic zone. The final feature used in classification of focal seizures is whether the focal seizure evolves to a bilateral tonic-clonic seizure. The term secondary generalized tonic-clonic seizure is no longer used because the term focal seizure more completely differentiates this type from generalized seizures.

Awareness is defined as knowledge and understanding that something is happening or exists. When a person is having a focal seizure, his or her awareness is determined by whether the person knows who they are and what is going on in his or her surroundings during the seizure; it does not refer to awareness of the seizure occurring. Awareness is also distinct from responsiveness. If awareness is impaired for any portion of the seizure, then the seizure is classified as a focal seizure with impaired awareness.

Awareness may be considered a surrogate for consciousness. Impaired awareness or consciousness during a seizure is likely secondary to depressed subcortical arousal systems, leading to deep sleep activity in widespread neocortical regions, hence the involvement of both subcortical and cortical structures. A focal aware seizure replaces the previously termed simple partial seizure, and a focal impaired awareness seizure replaces the term complex partial seizure. If unknown, the level of awareness does not need to be included.

Focal motor seizures can be more specifically defined. Motor-onset manifestations include automatisms, epileptic spasms, and atonic, clonic, hyperkinetic, myoclonic, or tonic seizures. Automatisms are coordinated, purposeless, repetitive motor activities that may appear normal in other circumstances. Examples include oral automatisms such as lip smacking and manual automatisms including repetitive hand movements such as patting (CASE 1-1).
Of note, automatisms can also be seen in absence seizures, which are discussed in the next section.

Focal atonic seizures are characterized by loss of tone in one body part. Clonic seizures are repeated, regularly spaced stereotypical jerking movements. Epileptic spasms were previously only considered generalized seizures. Clinically, epileptic spasms present in young children with flexion of the waist and flexion or extension of the arms, usually in clusters. If epileptic spasms occur in infants or early in life, they can be referred to as infantile spasms. Differentiating focal epileptic spasms from generalized epileptic spasms may require careful observation of clinical and electrographic features. Hyperkinetic or excessive muscular movement seizures can have variable features clinically, including thrashing or pedaling. Focal myoclonic seizures present with jerking but, in contrast to clonic seizures, the jerking is irregular and not rhythmic. Tonic seizures refer to motor seizures with increased tone or stiffening of the limb or neck.

Focal seizures with nonmotor symptoms as the first prominent feature include autonomic, behavior arrest, cognitive, emotional, or sensory seizures. Autonomic seizures present with changes in heart rate, blood pressure, sweating, skin color, piloerection, or gastrointestinal sensations. Behavioral arrest seizures are characterized by cessation of movement, which should be the dominant feature throughout the entire seizure and not just a brief part of the seizure; clinical symptoms include a blank stare and cessation from talking or moving. Patients with nonmotor cognitive seizures can experience changes in language function, thinking, or associated higher cortical functions; more specific examples include déjà vu, jamais vu (a feeling of unfamiliarity), or hallucinations. Emotional seizures appear with clear emotional changes such as dread, fear, anxiety, or pleasure. Focal sensory seizures are classified according to changes in sensory phenomena such as taste, smell, hearing, vision, pain, numbness, or tingling.

Focal seizures can be further classified as to whether they evolve to a bilateral tonic-clonic seizure. As discussed previously, this classification replaces secondary generalized tonic-clonic to avoid any confusion between generalized and focal seizures. These seizures start in one area of the brain (as with all focal seizures) and then spread to both sides of the brain. This spread is typically clearly seen on EEG.

Generalized Seizures

Similar to focal seizures, generalized seizures are classified according to motor or nonmotor manifestations. Broadly, motor seizures are either tonic-clonic or other motor seizures. Nonmotor generalized seizures primarily refer to absence seizures.

Motor onset more specifically includes tonic-clonic, clonic, tonic, myoclonic, myoclonic-tonic-clonic, myoclonic-atonic, atonic, or epileptic spasms. Generalized tonic-clonic seizures generally last 1 to 3 minutes and result in immediate loss of awareness or consciousness. The initial tonic phase is a stiffening of all limbs. The patient may groan or cry in the beginning as air is forced past the vocal cords. The tongue may also be bitten during this phase.

The clonic phase occurs after the tonic phase and is characterized by sustained rhythmic jerking of the limbs. If the person has impaired breathing, he or she may look dusky. Incontinence of either bladder or bowel occurs when the body...
relaxes. A generalized clonic seizure is characterized by bilateral and sustained rhythmic jerking. A patient with generalized tonic seizures will have stiffening of all limbs.

In contrast to generalized clonic seizures, generalized myoclonic seizures are associated with irregular and not necessarily synchronous bilateral jerking of limbs, face, eyes, or eyelids. Myoclonic-tonic-clonic seizures are a new seizure

**CASE 1-1**

A 27-year-old man presented after experiencing an episode of loss of awareness. His friend reported that he had been eating dinner when he acutely stared off, which was followed by lip smacking, chewing movements, and clenching of his left hand, lasting a total of 90 seconds. He then appeared confused and was back to baseline approximately 10 minutes after the episode began.

The patient’s past medical history was notable for a prolonged febrile seizure at age 18 months but was otherwise unremarkable. He took no medications and had no family history of seizures. He drank two to three glasses of wine a week. He denied tobacco or illicit drug use. Physical and neurologic examination were unremarkable. Brain MRI revealed atrophy of the right mesial temporal region and increased T2 signal in the right hippocampus (FIGURE 1-3). EEG revealed right temporal slowing and epileptiform sharp waves (FIGURE 1-4).

**COMMENT**

This patient’s clinical presentation was consistent with a focal seizure. His awareness was impaired, and early prominent features included nonmotor oral automatisms followed by motor left hand dystonia. This seizure would, therefore, be classified as a focal impaired awareness seizure with automatisms. The seizure combined with the MRI and EEG findings suggests a focal epilepsy with at least a 60% risk of having a second unprovoked seizure within 10 years. Specifically, this patient has right temporal lobe epilepsy, with right mesial temporal sclerosis as the etiology. Treatment with an antiepileptic medication should be recommended, and if he continues to have seizures despite treatment with two antiepileptic medications, he would be considered refractory, and referral to an epilepsy center for epilepsy surgery should be recommended.
designation and begin with irregular jerking on both sides followed by a tonic-clonic seizure. Myoclonic-tonic-clonic seizures are common in juvenile myoclonic epilepsy (CASE 1-2). Myoclonic-atonic seizures are also a new seizure designation and are characterized by an initial irregular jerking followed by loss of tone on both sides. These seizures are common in epilepsy with myoclonic-atonic seizures (Doose syndrome).
Atonic seizures are brief and occur when there is bilateral loss of tone and the muscles become limp. If the person is standing when the seizure occurs, he or she will fall, often resulting in injury. Epileptic spasms are also brief and typically occur in clusters with flexion at the trunk and flexion or extension of the limbs. As with focal epileptic spasms, an EEG may be needed to distinguish whether the seizure is generalized.

**CASE 1-2**

A 13-year-old girl presented for evaluation after experiencing a single generalized tonic-clonic seizure that occurred in the morning upon awakening. Her history revealed that for the past year, she would often drop her toothbrush in the morning.

Her past medical history and family history were unremarkable. Menarche had occurred at age 12. She took no medications and had no history of alcohol, tobacco, or illicit drug use. Her physical and neurologic examinations were unremarkable. Brain MRI was normal, and EEG revealed generalized spike-wave discharges (FIGURE 1-5). The patient’s parents questioned whether she had epilepsy and whether she should be treated.

![EEG of the patient in CASE 1-2. Longitudinal bipolar montage shows frontally predominant 3-Hz to 4-Hz generalized spike-wave discharges.](image)

**COMMENT**

Epilepsy is diagnosed if a person has one unprovoked seizure and at least a 60% risk of having a second unprovoked seizure within 10 years. This girl presented with a single generalized seizure with no focal features and had a history suggestive of morning myoclonus. The clinical presentation and EEG were consistent with a generalized epilepsy syndrome, likely juvenile myoclonic epilepsy. She was diagnosed with epilepsy, and antiepileptic drug treatment was recommended.
Nonmotor or absence seizures include typical, atypical, myoclonic, or eyelid myoclonia. Typical absence seizures present with a sudden cessation of activity sometimes with eye fluttering, head nodding, or other automatisms followed by an immediate recovery. EEG always reveals generalized spike-wave activity during the seizure. Atypical absence seizures are similar to absence seizures but have other features including slower onset, prolonged recovery, and more pronounced changes in tone. A myoclonic absence seizure begins with a few irregular jerks followed by an absence seizure. Eyelid myoclonia is defined by jerks of the eyelids and upward deviation of the eyes. Light and closing the eyes can precipitate these generalized seizures. Eyelid myoclonia with absence seizures is seen in Jeavons syndrome.

**Unknown Seizures**
Seizures of unknown onset can be classified by motor (tonic-clonic, epileptic spasms) or nonmotor (behavior arrest) presentations. If information is inadequate or if the seizure cannot be categorized, then the seizure is considered unclassified.

**UPDATED EPILEPSY CLASSIFICATION**
The second level of classification is the epilepsy type. This classification assumes the patient has epilepsy as defined by the previously discussed updated definition. The epilepsy type is predominantly determined clinically; characteristic EEG findings provide supportive evidence. Similar to seizure classification, the epilepsies are classified as generalized or focal. The new classification system additionally recognizes two new categories: combined generalized and focal epilepsy and unknown epilepsy.

Patients with generalized epilepsy have one or more of the generalized seizure types, and their EEGs typically display generalized spike-wave activity. For individuals who have generalized seizure types and a normal EEG, other data are needed to determine whether the epilepsy is generalized. Having myoclonic jerks or a pertinent family history supports the diagnosis of a generalized epilepsy type.

Clinically, patients with one or more focal seizure types have focal epilepsy. These epilepsies can be either unifocal or multifocal. Although not always seen, focal EEG findings such as focal slowing or epileptiform discharges support the diagnosis of focal epilepsy. Concordant focal MRI findings are also supportive.

Designation of combined generalized and focal epilepsy is for patients with both focal and generalized seizures. EEG may reveal both focal and generalized electrographic findings. Examples of combined generalized and focal epilepsy include Dravet syndrome and Lennox-Gastaut syndrome.

When the patient has epilepsy as defined by the ILAE but it remains undetermined whether the patient has focal or generalized epilepsy, the classification of unknown epilepsy type is used. Patients with this classification may not have an available EEG or the EEG may be indeterminate. Other supporting studies such as MRI and family history are also either not available or do not clarify the epilepsy classification.

**NEW CLASSIFICATION OF EPILEPSY SYNDROME**
The epilepsy syndrome is a new addition to the current classification system and is defined as “a cluster of features incorporating seizure types, EEG, and imaging..."
features that tend to occur together." Factors that contribute to epilepsy syndrome include age of onset, remission, triggers, diurnal variation, intellectual and psychiatric dysfunction, EEG findings, imaging studies, family history, and genetics. The ILAE has never formally classified a list of epilepsy syndromes; however, well-known and accepted syndromes are described, and some are reviewed here. For a full list of ILAE-accepted epilepsy syndromes, refer to the ILAE website.

Previously, the term *benign* was used to describe some of the epilepsy syndromes, but it is no longer used as it infers the epilepsy has minimal effect on the patient. It is now more clearly understood that any epilepsy can have social effects and can be associated with other comorbidities such as learning disorders or psychiatric conditions. The term *self-limiting* is now used.

**Idiopathic or Genetic Generalized Epilepsy Syndromes**

Idiopathic generalized epilepsies include childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy, and generalized tonic-clonic seizures alone (TABLE 1-1). Controversy surrounds the use of the term *idiopathic*, and removing it from epilepsy classification has been advocated. *Idiopathic* was meant to refer to *self* or *genetic*. There is, however, concern that use of the word *genetic* infers inherited, and many patients with epilepsy have de novo mutations or have complex genetic syndromes that occur with or without environmental factors. Many in the epilepsy community want to continue using the term *idiopathic generalized epilepsy*, and the ILAE task force decided to use it to refer to the previously mentioned epilepsies. When the clinician determines that a clear genetic etiology is present, the term *genetic generalized epilepsy* may be used to refer to the epilepsy syndrome. EEGs of the idiopathic generalized

<table>
<thead>
<tr>
<th>Epilepsy Syndrome</th>
<th>Seizure Types</th>
<th>Age of Onset</th>
<th>Self-limiting (Yes or No)</th>
<th>EEG Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood absence epilepsy</td>
<td>Absence, generalized tonic-clonic (rare)</td>
<td>4 to 10 years</td>
<td>Yes</td>
<td>Normal background, occipital intermittent rhythmic delta activity, 3–3.5 Hz generalized spike-wave discharges</td>
</tr>
<tr>
<td>Juvenile absence epilepsy</td>
<td>Absence, generalized tonic-clonic, myoclonic (rare)</td>
<td>Adolescence to early adulthood</td>
<td>No</td>
<td>Normal background, polyspikes may be present, 3–3.5 Hz generalized spike-wave discharges</td>
</tr>
<tr>
<td>Juvenile myoclonic epilepsy</td>
<td>Myoclonic, generalized tonic-clonic, absence (rare)</td>
<td>10 years to mid-twenties</td>
<td>No</td>
<td>Normal background, 3–3.5 Hz generalized spike-wave discharges, &gt;4 Hz generalized spike-wave discharges, high-amplitude polyspike-wave discharges with myoclonic seizures, photoparoxysmal response in up to 40% of patients</td>
</tr>
<tr>
<td>Epilepsy with generalized tonic-clonic seizures alone</td>
<td>Generalized tonic-clonic</td>
<td>Childhood to mid-adulthood</td>
<td>No</td>
<td>Normal background, generalized spike/polyspike-wave discharges</td>
</tr>
</tbody>
</table>
epilepsies reveal a normal electrographic background and characteristic generalized spike-wave findings (TABLE 1-1).18

Childhood absence epilepsy affects neurologically normal girls more than boys and is typically self-limiting. Onset is usually between 4 and 10 years of age, with remission usually occurring in adolescence. Patients present with absence seizures and occasionally with generalized tonic-clonic seizures. Early occurrence of generalized tonic-clonic seizures is associated with a poorer prognosis.

Juvenile absence epilepsy has onset in adolescence and early adulthood, with peak onset between 10 and 13 years of age. Girls and boys are affected equally. Absence seizures occur less frequently than in childhood absence epilepsy. Generalized tonic-clonic seizures occur early in the presentation, and myoclonic seizures, although rare, may also occur. In contrast to childhood absence epilepsy, this syndrome is not self-limiting.

Juvenile myoclonic epilepsy is one of the most typical epilepsy syndromes. Onset ranges from before age 10 through the mid-twenties and later in some cases. Juvenile myoclonic epilepsy occurs more commonly in women. All patients have myoclonic seizures and commonly have generalized tonic-clonic seizures. Absence seizures rarely occur. Most patients do not have spontaneous remission and require lifelong treatment with antiepileptic medication.

Epilepsy with generalized tonic-clonic seizures alone is characterized by presentation of generalized tonic-clonic seizures with an age range of childhood through mid-adulthood with peak onset in the second decade of life. Previously it was referred to as generalized tonic-clonic seizures upon awakening but was changed after recognition that seizures can occur at any time of day. Similar to juvenile absence epilepsy and juvenile myoclonic epilepsy, epilepsy with generalized tonic-clonic seizures alone is not self-limiting, and lifelong antiepileptic drug treatment is typically required.

Reflex Epilepsy Syndromes
Reflex epilepsy syndromes are epilepsies in which seizures are provoked by a specific stimulus. Seizures are typically generalized tonic-clonic seizures, but other generalized seizure types may also occur. Rarely, focal seizures may present as a reflex epilepsy. The most common reflex epilepsy syndrome is photosensitive epilepsy. Other reflex epilepsy syndromes include reading epilepsy and startle epilepsy.17,18

Focal Epilepsy Syndromes
Well-described focal epilepsy syndromes include childhood epilepsy with centrotemporal spikes and Panayiotopoulos syndrome. Previously, childhood epilepsy with centrotemporal spikes was referred to as benign epilepsy with centrotemporal spikes. Childhood epilepsy with centrotemporal spikes is a self-limited epilepsy that presents in the school years with brief focal motor hemifacial seizures and nocturnal focal motor seizures evolving to bilateral tonic-clonic seizures. EEG background is normal with sleep-activated centrotemporal spikes. Panayiotopoulos syndrome is also a self-limited epilepsy characterized by having focal autonomic seizures, often prolonged, and focal occipital high-amplitude sleep-activated spikes seen on EEG. Possible autonomic symptoms include vomiting, pallor, mydriasis, cardiorespiratory, gastrointestinal, and thermoregulatory symptoms, incontinence, and hypersalivation.19
EPILEPSY ETIOLOGY

The etiology of seizures and epilepsies is emphasized in the new classification system. In the prior classification system of the 1980s, etiology was inferred when classifying the epilepsy. *Idiopathic* primarily referred to genetic causes, *symptomatic* referred to the presence of a known disorder or lesion, and *cryptogenic* referred to a presumed but unknown symptomatic cause. As discussed, the term *idiopathic* is now used to refer to four well-described epilepsy syndromes. The terms *symptomatic* and *cryptogenic* are no longer used.

Six etiologic categories (structural, genetic, infectious, metabolic, immune, unknown) have been defined. When multiple potential etiologies are present, priority should be given to the etiology with more relevant management issues. Ongoing consideration of the etiology has clear implications for patient management as well as research efforts as we continue to study why patients develop seizures and we determine optimal treatments.

A structural etiology is determined when a structural abnormality is seen on neuroimaging and when the signs and symptoms of seizures, in combination with EEG data, suggest this abnormality is the probable cause of the seizures. If the clinical and EEG data are discordant with localization of the visible structural abnormality, then the imaging abnormality is not relevant to the patient’s epilepsy. Structural abnormalities may be genetic, acquired, or both. Possible structural abnormalities include stroke, trauma, tumor, malformations of cortical development, and infection.

Genetic etiologies are determined if there is a known or presumed genetic mutation in which seizures are a core symptom of the disorder. Genetic epilepsies are diverse, and the list grows each year. Importantly, genetic does not always mean inherited. Although some epilepsies are inherited, many occur secondary to a de novo (new) mutation in the affected individual. In some cases, the genetic mutation is not identified, but the clinical presentation, EEG findings, and family history suggest a genetic etiology. In addition, the genetic etiology for some epilepsy syndromes such as juvenile myoclonic epilepsy is inferred from research studies including twin and familial aggregation studies. Overall, genetic etiology is defined by having a known mutation, clinical presentation with supportive data and family history, or a syndrome with evidence from research studies to suggest a genetic etiology.

Infectious etiologies are the most common worldwide etiology. An important distinguishing point is that the patient has epilepsy secondary to an infectious etiology and not seizures in the setting of an acute infectious illness. Prototype infectious etiologies include neurocysticercosis, HIV, cytomegalovirus, and cerebral toxoplasmosis. Epilepsy onset secondary to a prior infectious insult such as meningitis or encephalitis is also considered an infectious etiology.

Epilepsies with a metabolic etiology occur secondary to a known or presumed metabolic disorder in which seizures are a core symptom of the disorder. Overlap with a genetic etiology may occur as many metabolic disorders have known genetic mutations. Of course, identifying a genetic etiology early in presentation is important because management interventions such as a change in diet or supplementation can affect its natural course.

Immune etiologies are increasingly recognized as potential causes of epilepsy. As with the other etiologies, seizures are a core symptom of the immune disorder. In patients with identified immune etiologies, immunotherapy should be considered. Examples of immune etiologies for seizures include...
anti-N-methyl-D-aspartate (anti-NMDA) receptor encephalitis and anti-leucine-rich, glioma inactivated 1 (anti-LGI1) encephalitis.

The last etiologic category is unknown; up to one-third of patients with epilepsy have no clear etiology. A cause likely exists, but its identification may be limited by inadequate resources such as poor access to up-to-date brain imaging, immune antibody testing, or genetic testing. It is hoped that with improved access to care as well as continued research into understanding the epilepsies the percentage of patients who have an unknown etiology will diminish and that the structure of the new classification system will provide a framework to better understand the epilepsies.

INCIDENCE OF EPILEPSIES AND ITS RELATION TO SEIZURE AND EPILEPSY CLASSIFICATION AND RISK FACTORS

The incidence of epilepsy is defined as the number of new epilepsy cases over a specified period of time. Incidence represents the number of new cases among susceptible persons in a given location and over a particular time span. Incidence studies, in contrast to prevalence studies, provide a better understanding of etiology and the natural history of epilepsy. Epilepsy incidence studies are, however, lacking and heterogeneous. Heterogeneity among reported incidence population studies may be addressed by use of universally adopted seizure and epilepsy classification systems. A well-constructed classification is needed for comparison among studies. The newly proposed 2017 ILAE classification system of seizures and the epilepsies provide a system that promotes standardization of terminology, which may lead to reduced variability among incidence studies and may, therefore, improve our understanding of seizure and epilepsy incidence. It has, however, also been argued that the system allows flexibility as cases may be classified in different categories depending on workup, creating a potential obstacle for epidemiologic studies.

The proposed 2017 epilepsy classification creates a framework to more specifically define the epilepsy, epilepsy syndrome, and etiology. The emphasis on etiology may lead to a better understanding and determination of epilepsy incidence, which, of course, depends on classification agreement among physicians. Universal implementation of this classification system and further study will hopefully clarify the utility of the newly proposed system and whether its use will reduce heterogeneity among incidence studies and allow us to better define significant factors that contribute to epilepsy incidence in all regions of the world.

CONCLUSION

Seizure and epilepsy classifications have evolved since a system was first introduced by Gastaut in the late 1960s. The 2017 ILAE classification of seizures, epilepsies, and epilepsy syndromes aims to group seizures according to clinical presentation and brain region onset and epilepsies according to seizure type, age of onset, probability of remission, EEG findings, radiologic findings, and genetics. An emphasis is now placed on etiology. Universal adoption and use of this classification system have direct implications on our understanding of epilepsy incidence. Multiple worldwide studies have found variable results with marked heterogeneity. In addition, incidence studies are limited in number and scope and rarely consider seizure type. Future studies using this standardized

KEY POINTS

- The etiology of seizures and epilepsies is emphasized in the 2017 International League Against Epilepsy classification system.
- A structural etiology is determined when a structural abnormality is seen on neuroimaging and when the signs and symptoms of seizures, in combination with EEG data, suggest this abnormality is the probable cause of the seizures.
- Genetic etiologies are determined if there is a known or presumed genetic mutation in which seizures are a core symptom of the disorder.
- Infectious etiologies are the most common worldwide etiology of epilepsy.
- Epilepsies with a metabolic etiology occur secondary to a known or presumed metabolic disorder in which seizures are a core symptom of the disorder.
- Immune etiologies are increasingly recognized as potential causes of epilepsy.
classification system will potentially clarify epilepsy incidence and hopefully reduce heterogeneity. In addition, further study is needed to evaluate the utility of the 2017 classification system. Although it establishes standard terminology, potential variability in coding and poor agreement among physicians may limit its use.

USEFUL WEBSITE

INTERNATIONAL LEAGUE AGAINST EPILEPSY

The International League Against Epilepsy (ILAE) is an international organization whose goals include advancement and dissemination of knowledge about epilepsy. The organization promotes research, education, and training and improves services and care for patients with epilepsy. Links to published articles on seizure and epilepsy classification are available on this website. epilepsydagnosis.org

REFERENCES


