Definition and Classification of Epilepsy

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Epilepsy Course for Neurological Residents
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Babylonian Cuneiform Tablet

- 1067-1046 B.C.
- The Sakikku (meaning All diseases)
- Many types of seizures were described
- Attributed to a certain demon or spirit


Definition

Epileptic seizure: a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain*


Epileptic seizure

Mode of onset – ‘transient’, demarcated in time, with a clear start and finish

Clinical manifestations – sensory, motor, and autonomic function; consciousness; emotional state; memory; cognition; and behavior

Ictogenesis - abnormal enhanced synchrony of neurones
Epilepsy: a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological and social consequences of this condition* requires the occurrence of at least one epileptic seizure.


Epileptic syndrome

- Group of clinical and EEG features common to patients with similar, but not necessarily identical etiologies
- Helps determine the appropriate therapy and the prognosis.

Epilepsy is a disease of the brain defined by any of the following conditions:

1. A least two unprovoked (or reflex) seizures occurring >24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years.
**Epilepsy definition 2014**

1. A least two unprovoked (or reflex) seizures occurring >24 h apart
   - is the same as the old definition of epilepsy
   - After a single unprovoked seizure, risk for another is 40-52%*. With two unprovoked non-febrile seizures, the chance by 4 years of having another seizure is 73%**.

** Hauser WA et al. NEJM1998;338:429-434.

2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
   - allows a condition to be considered epilepsy after one seizure if there is a high risk of having another seizure eg. the patient with a remote brain insult and an epileptiform EEG study.

3. Diagnosis of an epilepsy syndrome
   - If evidence exists for an epilepsy syndrome, then epilepsy may be presumed to be present, even if the risk of subsequent seizures is low eg., BECTS

Epilepsy is considered to be **RESOLVED** for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years.

- Being resolved does not guarantee that epilepsy will not return, but it means the chances are small and the person has a right to consider that she or he is free from epilepsy. This is a big potential benefit of the new definition.
Definition and Classification of Epilepsy 2017

**Epilepsy definition 2014**

The Treatment decision ≠ The diagnosis

: individualized depending upon the desires of the patient, the individual risk-benefit ratio and the available options

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**Epilepsy classification**

1. **For seizures**: represent the symptoms and signs in epileptology, rarely provide clue as to the underlying aetiology and prognosis

2. **For epilepsies and epileptic syndromes**: defined by electroclinical characteristics, sometimes determined by therapeutic and/or prognostic implication

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**Epilepsy classification**

- **1969** Gastaut proposed a classification of the epilepsies based on a combination of clinical and EEG data

- **1970** ILAE : International Classification of the Epilepsies (ICE)
  - Generalized (primary, secondary, undetermined)
  - Partial (all were presumed to be symptomatic)
  - Unclassifiable

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**ILAE Classification (ICE) 1981**

- **Partial-onset seizures**: begin in a focal area of the cerebral cortex
- **Generalized-onset seizures**: an onset recorded simultaneously in both cerebral hemispheres
- **Unclassified seizures**: seizures those are difficult to fit into a single class

The clinical diagnosis is difficult!

- Aura is a simple partial seizure.
- About 20-40% of auras have ictal correlation on the scalp EEG, most are not recorded well on a routine EEG.
- If aura > 30 minutes, considered as simple partial status epilepticus by definition but not in the classification.

In practice, assessing the patient's history whether consciousness was impaired is difficult.

- Patients might be able to remember their aura but are unaware that they were briefly unable to respond to the environment.
- CPS of frontal lobe origin may feature bizarre motor behaviors, might have a fast postictal recovery, and often appear in clusters.
- Nonepileptic seizures.

Clinically classifying a GTCs as being secondarily generalized (partial onset) or primarily generalized is difficult on the basis of the history alone.

- The aura preceding the secondarily generalized seizure is often forgotten because of postictal amnesia.
- Primarily generalized seizure.

- Absence vs. CPS.
ILAE Classification (ICEES) 1989

Syndromes were organized primarily according to

- **Mode of expression** (localization-related versus generalized)
- **Underlying cause** (idiopathic, symptomatic, and cryptogenic)


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Epileptic syndrome

- “benign” refers to prognosis, but some patients have subtle cognitive and behavioral disorders
- “idiopathic” refers to aetiology
- “generalized”: generalized seizure types and bilateral EEG abnormalities, but some patients have focal seizure clinical and EEG*

The Task Force on Classification and Terminology of ILAE 2001

• Axis 1: Ictal phenomenology: from the Glossary of Descriptive Ictal Terminology, can be used to describe ictal events with any degree of detail needed

• Axis 2: Seizure type: from the List of Epileptic Seizures. Localization within the brain and precipitating stimuli for reflex seizures should be specified when appropriate

The 2006 ILAE report

Epilepsy Syndromes by Age of Onset and Related Conditions

Neonatal period
- Benign familial neonatal seizures (BFNS)
- Early myoclonic encephalopathy (EME)
- Ohtahara syndrome

Infancy
- Migrating partial seizures of infancy
- West syndrome
- Myoclonic epilepsy in infancy (MEI)
- Benign infantile seizures
- Dravet syndrome
- Myoclonic encephalopathy in nonprogressive disorders

Engel J Jr. Epilepsia 2006;47:1558-68.
Epilepsy Syndromes by Age of Onset and Related Conditions

Adolescence
- Juvenile absence epilepsy (JAE)
- Juvenile myoclonic epilepsy (JME)
- Progressive myoclonic epilepsies (PME)

Less-specific age relationship
- Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)
- Familial temporal lobe epilepsies
- Familial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS)
- Rasmussen syndrome
- Gelastic seizures with hypothalamic hamartoma

Engel J Jr. Epilepsia 2006;47:1558-68.

Epilepsy Syndromes by Age of Onset and Related Conditions

Special epilepsy conditions
- Symptomatic focal epilepsies not otherwise specified
- Epilepsy with generalized tonic-clonic seizures only
- Reflex epilepsies
- Febrile seizures plus (FS+)
- Familial focal epilepsy with variable foci

Conditions with epileptic seizures that do not require a diagnosis of epilepsy
- Benign neonatal seizures (BSN)
- Febrile seizures (FS)

Engel J Jr. Epilepsia 2006;47:1558-68.

Epileptic syndrome

Debate!

- “Splitters”
- “Lumpers”

? Different and separate syndromes or different facets of a broader neurobiological spectrum of epilepsy
The 2010 ILAE report

**Focal seizures**
- For each seizure type, ictal onset is consistent from one seizure to another, with preferential propagation patterns that can involve the contralateral hemisphere.
- In some cases, more than one network, and more than one seizure type, but each individual seizure type has a consistent site of onset.


**Generalized seizures**
- "Originating at some point within, and rapidly engaging, bilaterally distributed networks which include cortical and subcortical structures, but not necessarily include the entire cortex.
- Generalized seizures can be asymmetric.

The 2010 ILAE report

**Generalized seizures**
- Tonic-clonic (in any combination)
  - Absence
    - Typical
    - Atypical
  - Absence with special features
    - Myoclonic absence
    - Atonic absence

**Focal seizures**
- Unknown
  - Epileptic spasms

**Absence**
- Typical
- Atypical
- Absence with special features
  - Myoclonic absence
  - Myoclonic myoclonic
  - Myoclonic atonic
  - Myoclonic tonic

**Clonic**
- Tonic
- Atonic

*Seizures that cannot be clearly diagnosed into one of the preceding categories should be considered unclassified until further information allows their accurate diagnosis.*

*This is not considered a classification category, however.*

The 2010 ILAE report

Replaced the terms “idiopathic,” “symptomatic,” and “cryptogenic” with the following:

- **Genetic:** “the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of the disorder, but the possibility that environmental factors contribute to expression of the disease is not excluded.”

- **Structural metabolic:** “there is a distinct other structural or metabolic condition or disease that has been demonstrated to be associated with a substantially increased risk of developing epilepsy in appropriately designed studies.” These disturbances can be acquired or genetic (e.g., tuberous sclerosis).

- **Unknown cause**
The 2010 ILAE report
Electroclinical syndromes and other epilepsies

**Electroclinical syndromes arranged by age at onset**

**Neonatal period**
- Benign familial neonatal epilepsy (BFNE)
- Early myoclonic encephalopathy (EME)
- Ohtahara syndrome

**Infancy**
- Epilepsy of infancy with migrating focal seizures
- West syndrome
- Myoclonic epilepsy in infancy (MEI)
- Benign infantile epilepsy
- Dravet syndrome
- Myoclonic encephalopathy in nonprogressive disorders

**Childhood**
- Febrile seizures plus (FS+)
  (can start in infancy)
- Panayiotopoulos syndrome
- Epilepsy with myoclonic atonic (previously ataxic) seizures
- Benign epilepsy with centrotemporal spikes (BECTS)
- AUTS
- Landau-Kleffner syndrome (LKS)
- Childhood absence epilepsy (CAE)
- Benign neonatal seizures (BNS)
- Febrile seizures (FS)

**Epilepsies attributed to and organized by structural-metabolic causes**
- Malformations of cortical development (hemimegalencephaly, heterotopias, etc.)
- Neurocutaneous syndromes (tuberous sclerosis complex, Sturge-Weber, etc.)
- Tumor
- Infection
- Trauma
- Angioma
- Perinatal insults
- Stroke
- Etc.

**Epilepsies of unknown cause**
- Conditions with epileptic seizures that are traditionally not diagnosed as a form of epilepsy per se.
- Benign neonatal seizures (BNS)
- Febrile seizures (FS)
Definition

**Epileptic seizure type**

An ictal event believed to represent a unique pathophysiological mechanism and anatomical substrate. This is a diagnostic entity with etiologic, therapeutic, and prognostic implications. *(new concept)*

**Epilepsy syndrome**

A complex of signs and symptoms that define a unique epilepsy condition with different etiologies. This must involve more than just the seizure type; thus, frontal lobe seizures, for instance, do not constitute a syndrome. *(changed concept)*

**Epilepsy disease**

A pathologic condition with a single, specific, well-defined etiology. Thus, progressive myoclonus epilepsy is a syndrome, but Unverricht-Lundborg is a disease. *(new concept)*

**Epileptic encephalopathy**

A condition in which the epileptiform abnormalities themselves are believed to contribute to the progressive disturbance in cerebral function. *(new concept)*
**Definition**

**Benign epilepsy syndrome**

A syndrome characterized by epileptic seizures that are easily treated, or require no treatment, and remit without sequelae.

However, the use of this term is discouraged in the 2010 report because of new data revealing cognitive deficits in some of these conditions. *(clarified concept)*

**Reflex epilepsy syndrome**

A syndrome in which all epileptic seizures are precipitated by sensory stimuli.

Isolated reflex seizures can also occur in situations that do not necessarily require a diagnosis of epilepsy.

Seizures precipitated by other special circumstances, such as fever or alcohol withdrawal, are not reflex seizures. *(changed concept)*

**The 2017 ILAE Classification**

- **Level 1**: Seizure type
- **Level 2**: Epilepsy based on seizure type
- **Level 3**: Epileptic syndrome
- **Level 4**: Epilepsy with etiology
The New Basic Classification

Based on 3 key features

- Where seizures begin in the brain
- Level of awareness during a seizure
- Other features of seizures

Defining Where Seizures Begin

The type of seizure onset affects choice of seizure medication, possibilities for epilepsy surgery, outlook, and possible causes.

1. Focal seizures: Previously called partial seizures, these start in an area or network of cells on one side of the brain.

2. Generalized seizures: Previously called primary generalized
   - Engage or involve networks on both sides of the brain at the onset.

3. Unknown onset
   - Later on, the seizures type can be changed if the beginning of a person's seizures becomes clear.

4. Focal to bilateral seizure: Previously called partial seizures with secondary generalized seizures
   - Now the term generalized refers only to the start of a seizure
   - The new term for secondary generalized seizure would be a focal to bilateral seizure.
One of the main factors affecting a person’s safety during a seizure. Awareness is used instead of consciousness, because it is simpler to evaluate.

1. Focal aware seizure:
   - Intact awareness, even if unable to talk or respond during a seizure
   - This replaces the term simple partial.

2. Focal impaired awareness seizure
   - This replaces the term complex partial seizure.

3. Awareness unknown
   - Sometimes it’s not possible to know if a person is aware or not
   - For example if a person lives alone or has seizures only at night.

4. Generalized seizures:
   - All presumed to affect a person’s awareness or consciousness in some way
   - Thus no special terms are needed to describe awareness in generalized seizures.
Describing Motor and Other Symptoms in Focal Seizures

1. Focal motor seizure
   - Some type of movement occurs during the event e.g., twitching, jerking, or stiffening movements of a body part or automatisms (automatic movements such as licking lips, rubbing hands, walking, or running)

Describing Motor and Other Symptoms in Focal Seizures

2. Focal non-motor seizure
   - Has other symptoms that occur first, such as changes in sensation, emotions, thinking, or experiences.
   - Also possible for a focal aware or impaired awareness seizure to be sub-classified as motor or non-motor onset.

Describing Motor and Other Symptoms in Focal Seizures

3. Auras
   - The term aura to describe symptoms a person may feel in the beginning of a seizure is not in the new classification
   - These early symptoms may be the start of a seizure.

Describing Generalized Onset Seizures

1. Generalized motor seizure
   - The generalized tonic-clonic seizure term is still used to describe seizures with stiffening (tonic) and jerking (clonic)
   - This loosely corresponds to “grand mal.”
   - Many of these terms have not changed and a few new terms have been added
Describing Generalized Onset Seizures

2. Generalized non-motor seizure

- These are primarily absence seizures and the term corresponds to the old term “petit mal.”
- Involve brief changes in awareness, staring, and some may have automatic or repeated movements like lip smacking.

Some other points

- The new classification is designed to have some flexibility. Use of other descriptive terms or even free text is encouraged.

- Most seizures can be classified by signs and symptoms that happen during a seizure. However, other information is useful when available: phone videos, EEG, MRI, and other brain imaging, blood tests, or gene tests.
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