Classification of Epilepsy: What's new?

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Current as at February 2022

The following teaching session and associated written information provides education for neurological problems. Every effort has been made to ensure the information is current at the time presented.

Use of the information and its application to the care of the individual patient and their tailored management, however, remains at the sole discretion of the treating physician and should always be adapted to meet the needs of the individual patient.

For confidentiality, please DO NOT RECORD these sessions.

Handouts will be provided after each session.

Thankyou.

New Epilepsy Classification

- The following material on the new epilepsy classification is based on the following 3 papers:
  - Scheffer et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia, 58(4): 512-521,2017.
  - Fisher et al. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. Epilepsia, 2017, 58(4): 522-530
  - Fisher et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia, 58(4): 531-542, 2017.

Proposal for a Framework for Epilepsy Classification and Diagnosis

- Allows diagnosis at multiple levels
- Classification is primarily for clinical purposes and is relevant in all environments.
- Inherently dynamic

What are the criteria for the diagnosis of epilepsy

Operational (practical) definition of Epilepsy. ILAE, 2014

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

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

When can I say I no longer have epilepsy

Epilepsy Resolved

Epilepsy is now considered resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age

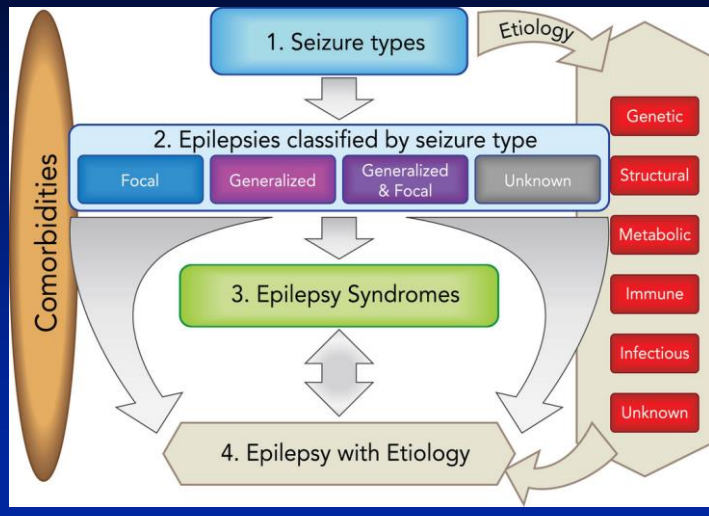
Or

those who have remained seizure free for past 10 years

with no seizure medicines for last 5 years.

Framework for epilepsy classification

Epilepsia 2017,58(4)512-21



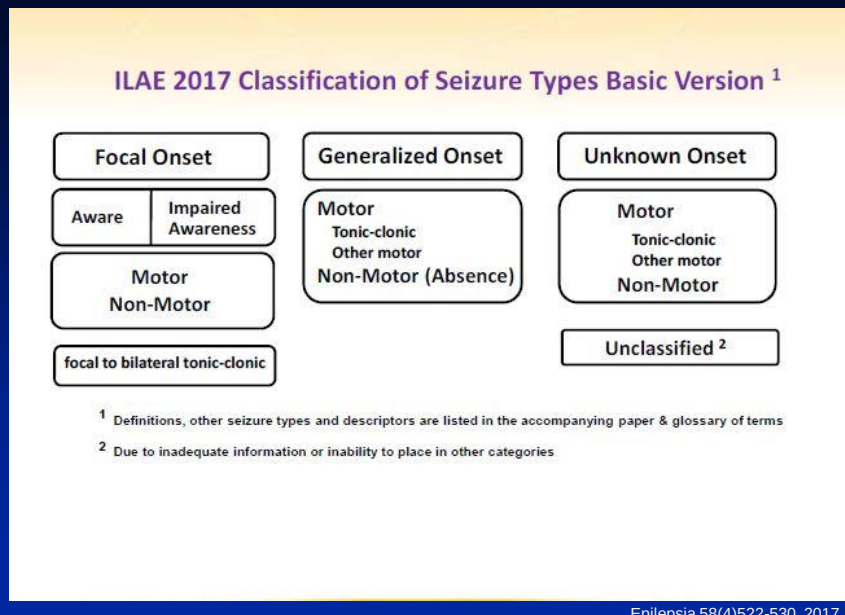
Framework of Epilepsy classification

First Step:

What is the seizure type?

Mode of seizure onset and classification of seizures

- **Focal seizures** originate within networks limited to one hemisphere.
  - For each seizure type ictal onset is consistent from one seizure to another, with propagation patterns that can involve the contralateral hemisphere.
- **Generalized epilepsies** are within, and rapidly engage bilateral distributed networks.
  - Can include cortical and subcortical structures, but not necessarily include entire cortex
  - Generalized seizures may appear asymmetric
- Maybe of Unknown Onset.



Epilepsia 58(4)522-530, 2017

Descriptors of focal seizures according to degree of impairment during seizure

- Key role of **Awareness** in seizure classification because of practical importance for
  - Driving
  - Safety during seizures
  - Interference with schooling and learning

- **Classification uses Awareness as seizure name**
  - Focal seizure with awareness: replaces Simple Partial Seizure
  - Focal seizure with impaired awareness: Replaces Complex Partial Seizure

Spread of focal seizure

Evolving to a bilateral convulsive seizure

- May include tonic, clonic or tonic and clonic components in any order

- Replaces term “secondarily generalized seizure”

- Example: Focal motor left face/ arm/leg → bilateral convulsive

ILAE 2017 Classification of Seizure Types Expanded Version[1]

Focal Onset

Aware | Impaired Awareness

Motor Onset
- automatisms
- atonic[2]
- clonic
- epileptic spasms[2]
- hyperkinetic
- myoclonic
- tonic

Non-Motor Onset
- autonomic
- behavior arrest
- cognitive
- emotional
- sensory

focal to bilateral tonic-clonic

Generalized Onset

Motor
- tonic-clonic
- clonic
- tonic
- myoclonic
- myoclonic-tonic-clonic
- myoclonic-atonic
- atonic
- epileptic spasms[2]

Non-Motor (absence)
- typical
- atypical
- myoclonic
- eyelid myoclonia

Unknown Onset

Motor
- tonic-clonic
- epileptic spasms

Non-Motor
- behavior arrest

Unclassified[3]

1 Definitions, other seizure types and descriptors are listed in the accompanying paper and glossary of terms.

2 These could be focal or generalized, with or without alteration of awareness

3 Due to inadequate information or inability to place in other categories

Epilepsia 58(4) 522-30 2017

Framework for epilepsy classification

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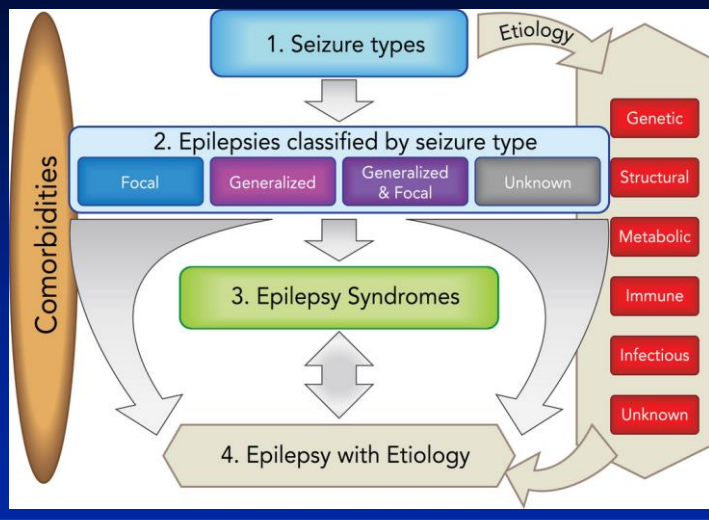


Framework of Epilepsy Classification

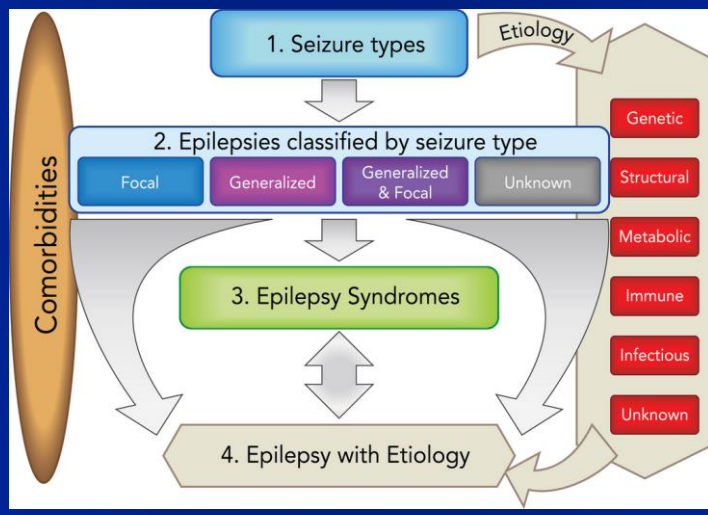
- **Step 2: Epilepsies classified by seizure type:**
  - Generalized Seizures
  - Focal Seizures
  - Generalized and Focal
  - Unknown

Epilepsy Type

- **Generalized epilepsy:**
  - Range of seizures types
  - Generalized spike and wave on EEG (need supportive evidence in patient with generalized tonic clonic seizures.)
- **Focal epilepsies**:
  - Unifocal, multifocal, one hemisphere.
  - EEG: focal epileptiform discharges
- **Combined generalized and focal:**
  - Diagnosis made on clinical grounds
  - Dravet and Lennox Gastaut Syndromes
- **Unknown:**
  - Incomplete data or data non informative.
  - Example: 5years old with 2 symmetrical tonic clonic seizures, normal EEG

Framework for epilepsy classification

***Epilepsia* 2017,58(4)512-21**



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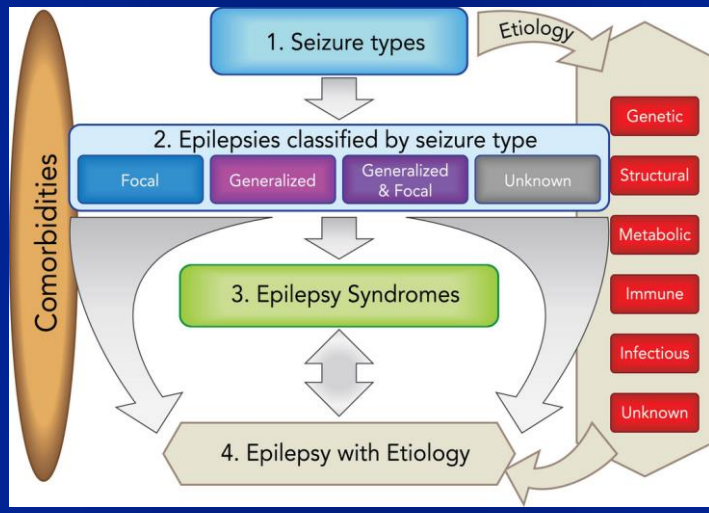
Framework of Epilepsy classification

- **Step 3: Diagnosis based on Syndrome**
- Distinctive clinical entities that carry treatment and prognostic implications.
- Can be classified according to age:
  - Neonatal e.g. Self limited familial neonatal epilepsy
  - Infancy: e.g. Dravet syndrome
  - Childhood: e.g. Self-limited epilepsy with centrotemporal spikes
  - Adolescence: e.g. Juvenile myoclonic epilepsy
- The arrangement of syndromes does not reflect aetiology.
- Syndromes may have range of aetiologies eg West syndrome.

Framework for epilepsy classification

Epilepsia **2017,58(4)512-21**



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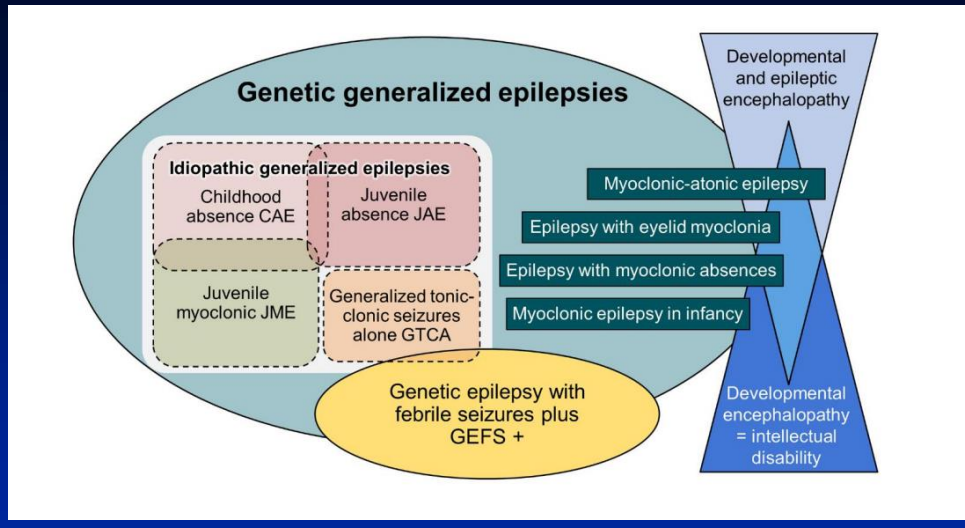
The epilepsy diagnosis

- **<u>Step 4: Based on Aetiology</u>:**
  - Genetic
  - Structural
  - Metabolic
  - Immune
  - Infectious
  - Unknown

Changes in Terminology: the term "Genetic" [1]

- **'*Genetic*' replaces '*Idiopathic*' but term idiopathic retained in 2022 as subgroup of Genetic Generalized Epilepsies for 4 common syndromes** (JME, CAE, JAE, GTCA.)
  - This does not mean that underlying genetic mutation is known or inherited
  - Specific genetic mutations are known in only a small minority of patients with epilepsy
  - De novo mutations are found increasingly. Explains lack of family history.
  - A genetic mutation maybe inherited but not fully penetrant.
  - Complex inheritance maybe present. Several genes contribute to risk. Susceptibility variants.
  - In most instances term "genetic" denotes that twin and family studies provide strong evidence for genetic basis. Here genes not usually known.

Reference: [1] Epilepsia 2017,58(4), 512-21



Concept of Genetic Generalized Epilepsy versus Idiopathic Generalized Epilepsy (ILAE 2022)

Framework for epilepsy classification[1]

- In some cultures use of word “genetic” not acceptable: use phrase “of unknown aetiology”.
- Genetic causes maybe associated with several epilepsy syndromes.
- Increasing number of genetic abnormalities causing both severe and mild epilepsies – SCNIA (Dravet and GEFS+). Mosaicism.
- In many incidences multiple aetiologies apply e.g. Tuberous Sclerosis : structural and genetic.
  - Provide 2 diverse treatment paths.

Reference: [1] Scheffer et.al Epilepsia 2017,58(4),512-521

Aetiology: Structural

- Need for careful imaging
  - Cortical malformation e.g. bottom of sulcus dysplasia
  - Hypothalamic hamartoma
  - Double cortex
- Underlying cause of abnormality maybe genetic or acquired - polymicrogyri
  - Secondary to gene mutation - GPR56. Aetiology: Genetic/Structural
  - Intrauterine CMV
  - Vascular insult

Terminology changes

- **In:**
  - Developmental and Epileptic Encephalopathy
- **Out:**
  - Symptomatic generalized
  - Benign

Developmental and epileptic encephalopathies

- **Epileptic encephalopathy:**
  - Epileptic activity itself contributes to severe cognitive and behavioural impairments above and beyond what might be expected from underlying pathology.
  - Global or selective impairments can be seen along a spectrum of severity and across all epilepsies.
- **Developmental encephalopathy:**
  - Developmental impairment without frequent epileptiform activity.
- Concept of two entities important for parents and their expectations.

The term " Benign"

- Use of this term underestimates comorbidities that maybe associated with "milder" epilepsies such as BRE, CAE.
- New terms suggested:
  - Self limited
  - Pharmacoresponsive
- Terms such as catastrophic and malignant have been abandoned.

Case Example

4m (F)

- Description from discharge summary:
  - Presented to country hospital multiple seizures - lip smacking, eye rolling, staring, floppy, generalized tonic clonic activity with duskiness, 1 minute events. Post ictal drowsiness.
  - No family history. Normal exam. Given phenytoin and keppra loads with good effect. Normal MRI. Discharged keppra.
- 4 days later:
  - Multiple seizure recurrence, 50 daily.
  - History emerged father (tonic clonic seizures), paternal grandmother and aunt had seizures at same age. All had good outcome with seizure freedom second year of life.
- EEG normal
- Treated low dose topimax and low dose tegretol. No further seizures. Withdrawal of medicines at 12 months seizure freedom.

Case: Epilepsy diagnosis and classification

- **Seizure type:**
  - Focal with loss of awareness, evolving to bilateral convulsive.
- **Epilepsy based on seizure type:**
  - Focal
- **Syndrome:**
  - Self limiting infantile familial convulsions.
- **Aetiology:**
  - Genetic SCN2A gene mutation.
  - Second commonest syndrome after West syndrome, 12 months[1]

Reference: [1]Epilepsia 2016, 57,10, 1594-1601

Framework for epilepsy classification

***Epilepsia* 2017,58(4)512-21**