Classification of Epilepsy: What's new?

A/Professor Annie Bye

Current as at January 2021

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

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%) after two unprovoked seizures, occurring over the next 10 years.

3. Diagnosis of an epilepsy syndrome.

Epilepsy Resolved

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

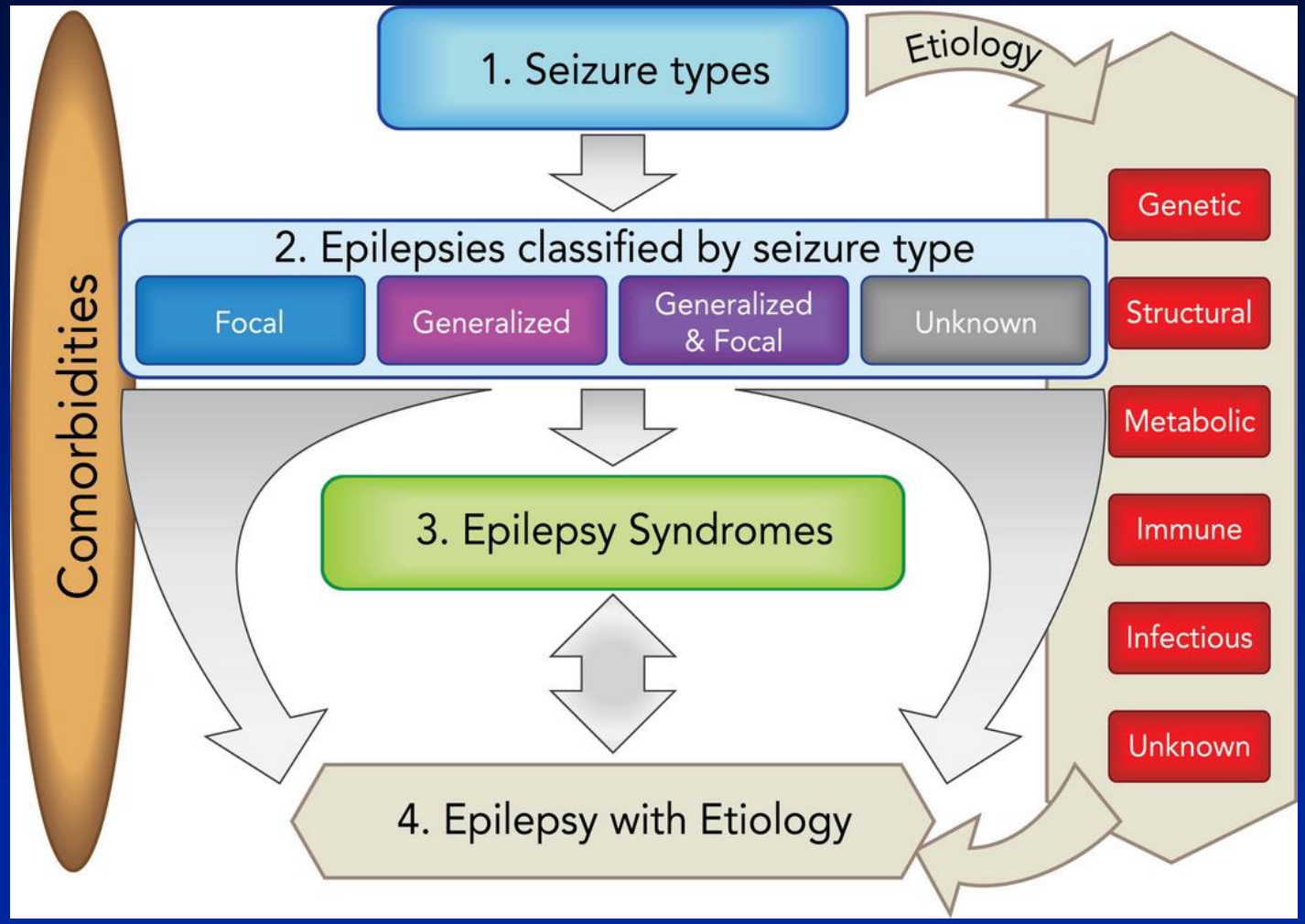
Or

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

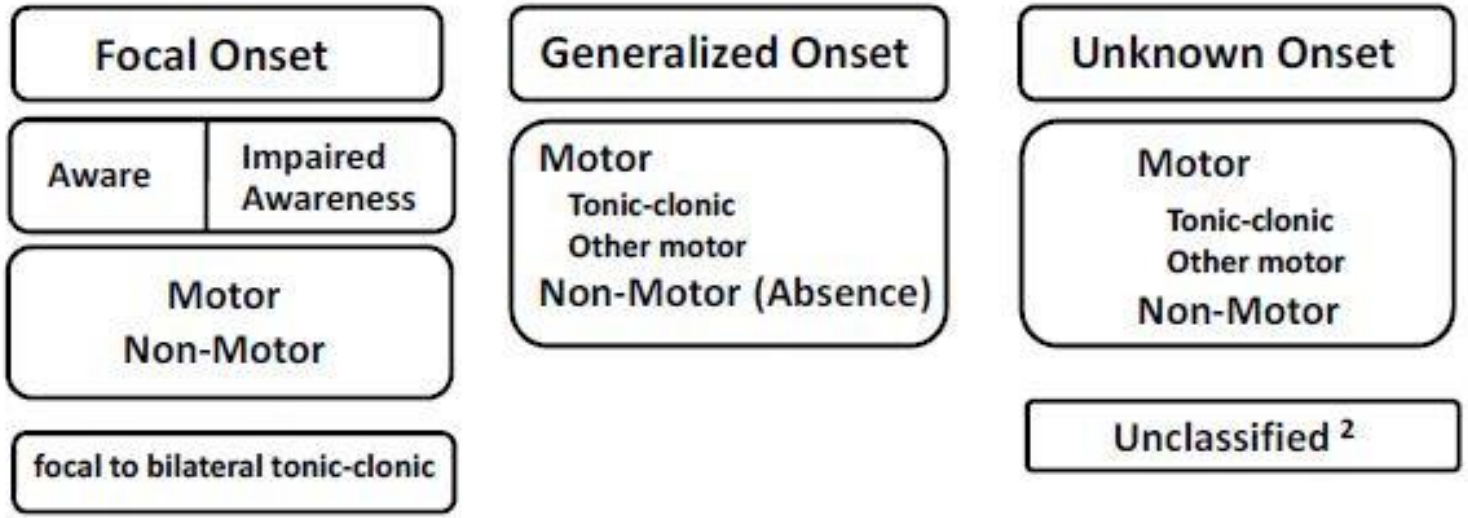
First Step:

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.

ILAE 2017 Classification of Seizure Types Basic Version [1]



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

[2] Due to inadequate information or inability to place in other categories

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

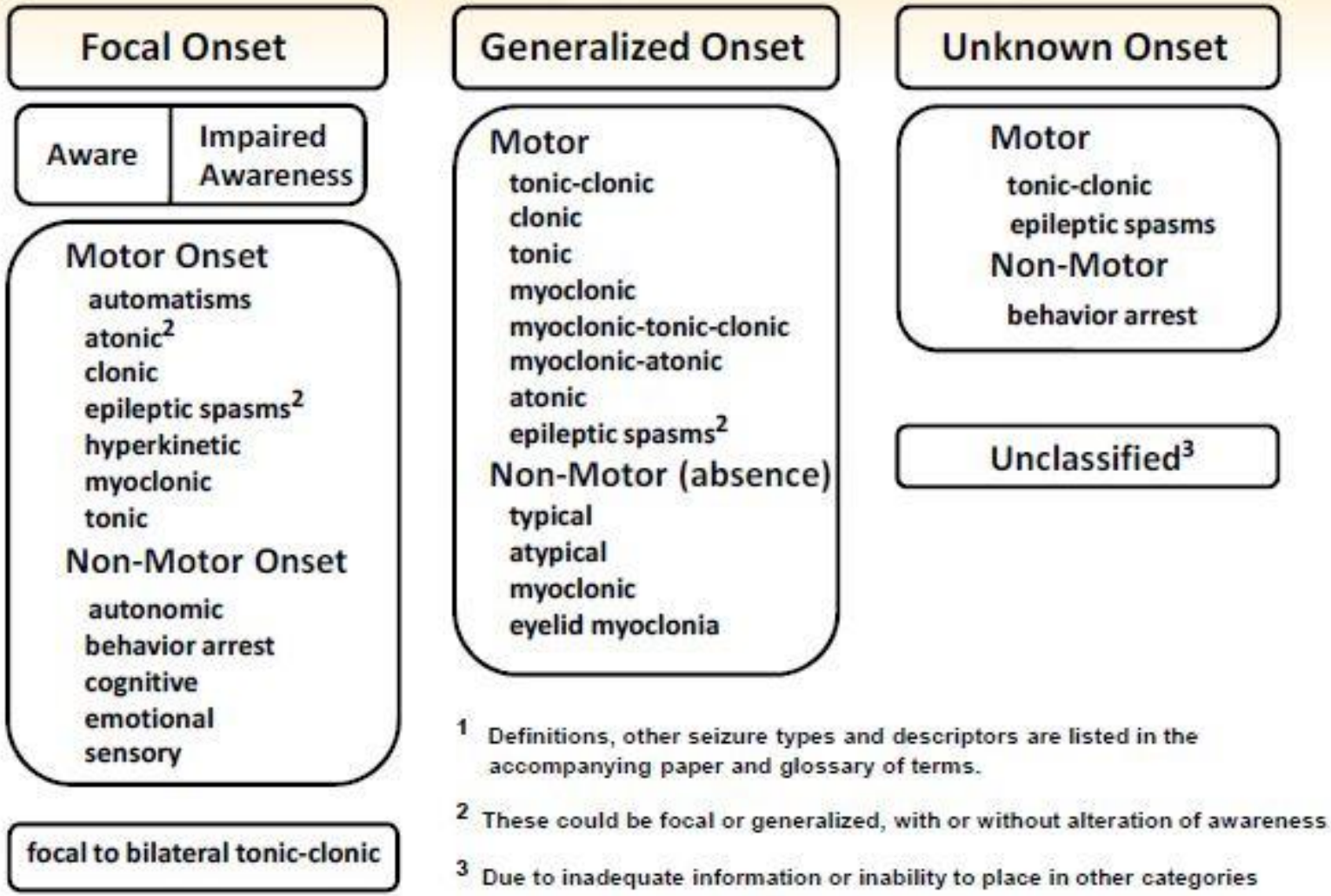
- **Classification uses Awareness as seizure name**
  - Focal seizure with awareness: replaces Simple Partial Seizure
  - Focal seizure with impaired awareness: Replaces Complex Partial Seizure

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]



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

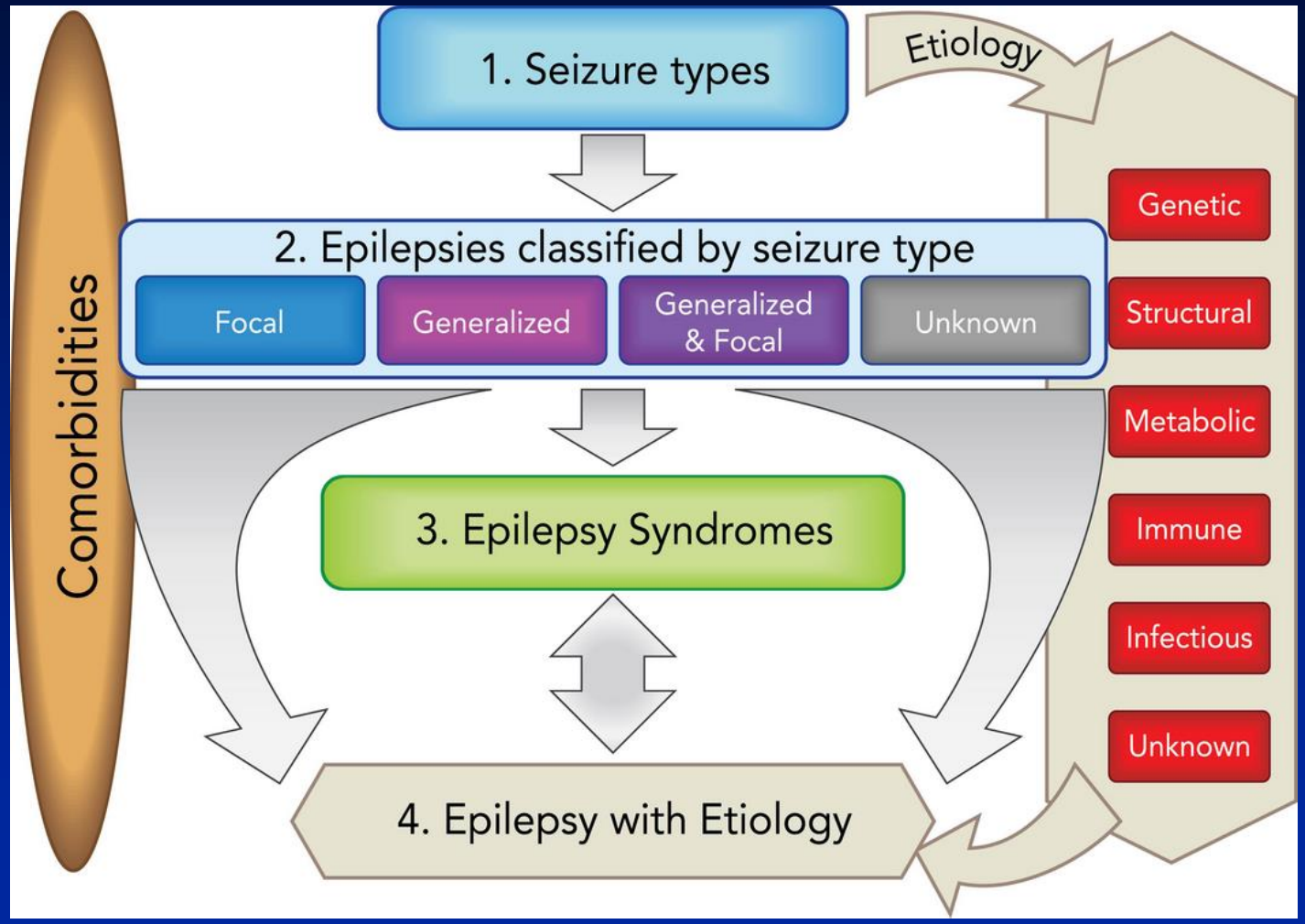
2 These could be focal or generalized, with or without alteration of awareness

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

Epilepsia 58(4) 522-30 2017

Framework for epilepsy classification

Epilepsia 2017,58(4)512-21



Framework of Epilepsy Classification

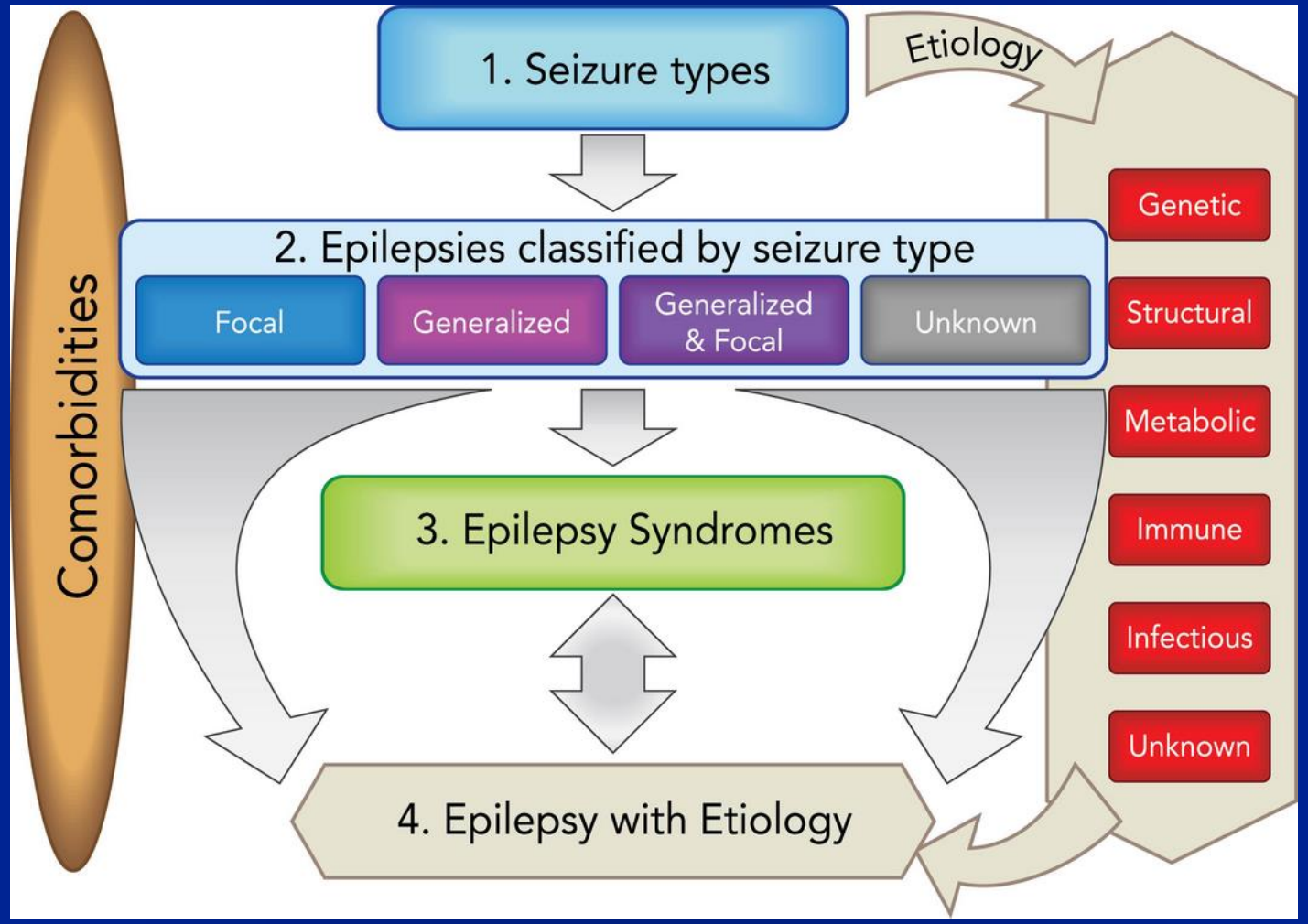
- **Step 2: Epilepsies classified by seizure type:**
  - Generalized Seizures
  - Focal Seizures
  - Generalized and Focal
  - Unknown

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



Framework of Epilepsy classification

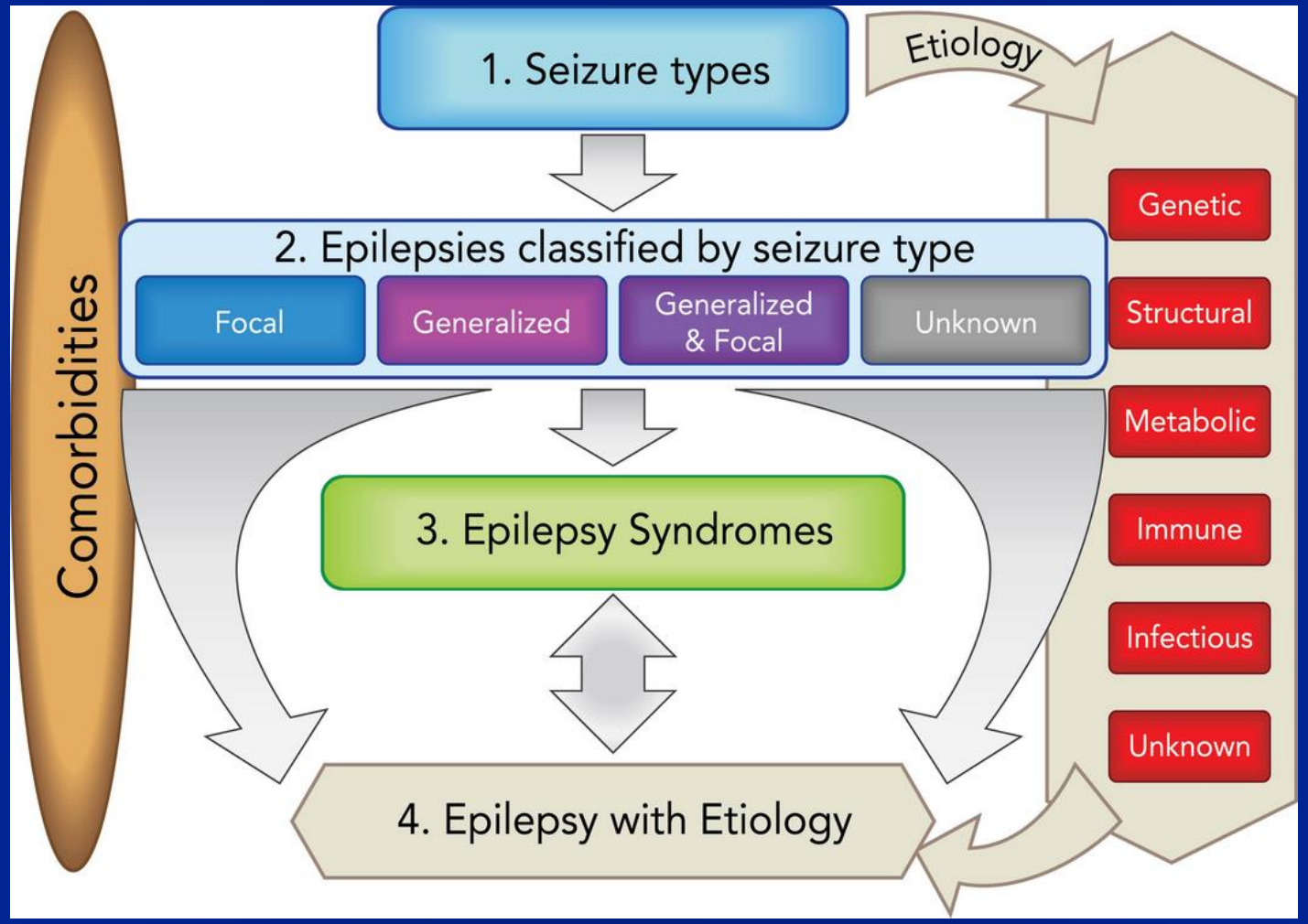
- **Step 3: Diagnosis based on Syndrome**
- Distinctive clinical entities that carry treatment and prognostic implications.

- 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



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**.
  - 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

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 eg 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

New terms:

- Developmental and Epileptic Encephalopathy

- **Old terms:**
  - 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.

Framework for epilepsy classification

Epilepsia 2017,58(4)512-21