DEFINITION AND CLASSIFICATION OF EPILEPSY

KAMORNWAN KATANYUWONG MD.

5th epilepsy camp 2014 : Ayutthaya

OUTLINE

- Definition of epilepsy
  - *Definition of seizure*
- Epilepsy classification
- Test

DEFINITION OF EPILEPSY

Glossary of Descriptive Terminology for Ictal Semiology: Report of the ILAE Task Force on Classification and Terminology

Epilepsia 2001

Special Article

Epileptic Seizures and Epilepsy: Definitions Proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE)

Epilepsia 2005

An Operational Clinical Definition of Epilepsy

ILAE website 2013

A practical clinical definition of epilepsy

Epilepsia 2014

SEIZURE

- **Greek** : meaning ***to take hold***
- **Modern** : sudden and severe event
- **Seizure = epileptic seizure**
- *Cardiology : heart seizure*

2001

I GENERAL TERMS

1.0 SEMIOLOGY
That branch of linguistics concerned with signs and symptoms.

2.0 EPILEPTIC SEIZURE
Manifestation(s) of epileptic (excessive and/or hypersynchronous), usually self-limited activity of neurons in the brain.

3.0 ICTUS
A sudden neurologic occurrence such as a stroke or an epileptic seizure.

4.0 EPILEPSY

a) Epileptic Disorder: A chronic neurologic condition characterized by recurrent epileptic seizures.
b) Epilepsies: Those conditions involving chronic recurrent epileptic seizures that can be considered epileptic disorders.

2005: EPILEPSY

- A **disorder** of the brain characterized by enduring predisposition to generate epileptic seizure
- Usually practically applied as having 2 unprovoked seizures more than 24 hours apart

2005

Table 1: Conceptual Definition of Seizure and Epilepsy – 2005 Report

An **epileptic seizure** is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

Epilepsy is 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. The definition of epilepsy requires the occurrence of at least one epileptic seizure.

2005: ELEMENTS OF A DEFINITION OF EPILEPSY

- History of at least one seizure
- Enduring alteration in the brain that increase the likelihood of future seizures
- Associated neurobiologic, cognitive, psychological and social disturbances

2013: EPILEPSY

A **disease** of the brain defined by any of the following conditions

1. At least 2 unprovoked seizures occurring more than 24 hours apart
2. One unprovoked seizure and a probability of further seizures similar to the general recurrence risk after two unprovoked seizures (approx 75% or more)

2013

- *Epilepsy presents after 2 unprovoked seizures occurring at least 24 hours apart (Hauser et al 1991)*
- After 2 unprovoked non-febrile seizure, the chance of having another is 73% (Hauser et al 1998) at 4 years
- After a single unprovoked seizure, the chance of having another is 40-52% (Berg&Shinnar 1991)

2013

Q: Why 24 hours apart ?

A: if seizures clustering within 24 hours ⇨risk factor for later seizures = risk after a single seizure

2013

- Stroke, CNS infection and trauma is important
- If the patient has a single unprovoked seizure after a remote brain insult ⇨ risk of a second unprovoked seizure = risk for further seizures after two unprovoked seizures

2013

- Some patient with a single unprovoked seizure in a circumstance of an epilepsy syndrome
  - ⇨ high risk of recurrence
  - ⇨ epilepsy

No longer present ≠ cure

2013: EPILEPSY

Epilepsy is considered **to be no longer present** for

- individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or
- those who have remained seizure-free for at least 10 years off AEDs
- No known risk factors associated with a high probability (≥ 75%) of future seizure

2013

- Cure = disappearance
- Remission = abeyance of a disease
- " no longer present" = the person no longer has epilepsy, although it does not guarantee that it will not return

2014

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

Epilepsia 2014

2013 = no longer present

2014

Resolved

- Had age-dependent epilepsy syndrome but are now past the applicable age
- Seizure free for at least 10 years and off AEDs for at least the last 5 years

2013 sz free 10 yrs off AED

Resolved is not identical to remission or cure

2014

- A decision for treatment does not equate to a diagnosis of epilepsy
- A diagnosis of epilepsy does not require treatment

2013, 2014

- 2005: Epilepsy = Disorder

Functional, not lasting

- 2013 : Epilepsy = Disease
- 2014: Epilepsy = Disease

2014

- When a diagnosis of epilepsy remains uncertain…
- A condition called " probable" (or possible) epilepsy
- *You have probable epilepsy* ***VS***
  You probably have epilepsy

NEW DEFINITION

- ? Affect prevalence of epilepsy
- Making the clinicians more comfortable in initiating treatment after some unprovoked seizures
- Required specialized diagnostic and interpretative skills- esp in ***assessing recurrence risks*** or in ***diagnosing syndromes***

CLASSIFICATION

WHY CLASSIFICATION IS NEEDED ?

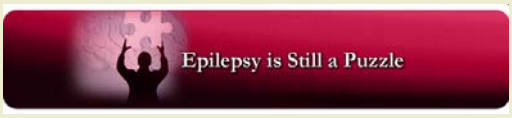
- A universal vocabulary that facilitated communication among clinicians
- Also established a taxonomy foundation for the research on epilepsy

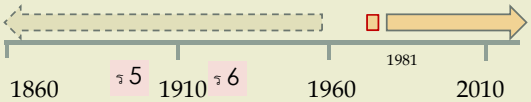
In general

TYPES OF CLASSIFICATION

- Biology:
- Etiology: 1^0 (idiopathic) or 2^0 (symptomatic)
- Pathology: Cancer
- Imaging: Cortical dysplasia
- Clinical criteria e.g. age onset, disease course, distribution of symptoms: HA
- Mixed:

OVER THE PAST 150 YEARS





COMMISSION ON CLASSIFICATION AND TERMINOLOGY OF ILAE

- Classification of Epileptic Seizures in 1981
- Classification of Epilepsies and Epileptic syndromes in 1989
- A proposed diagnostic scheme for people with epileptic seizures and with epilepsy : Report of the ILAE Task Force on Classification and Terminology in 2001
- ….2006,……2010

2010…2013…THE WINNER

2005-2009

ILAE CLASSIFICATION WORKING GROUP

Epilepsia, 51(4):676–685, 2010
doi: 10.1111/j.1528-1167.2010.02522.x

SPECIAL REPORT

Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009

*†Anne T. Berg, ‡Samuel F. Berkovic, §Martin J. Brodie, ¶Jeffrey Buchhalter, #**J. Helen Cross, ††Walter van Emde Boas, ‡‡Jerome Engel, §§Jacqueline French, ¶¶Tracy A. Glauser, ##Gary W. Mathern, ***Solomon L. Moshé, †Douglas Nordli, †††Perrine Plouin, and ‡Ingrid E. Scheffer

THE CLASSIFICATION CRITERIA OF

Epilepsies (Merlis 1970)	Epileptic seizures (Gastuat 1970)
• Clinical criteria Seizures Neurologic status Age of onset Etiology • EEG criteria Interictal EEG Ictal EEG	• Clinical seizure type • EEG seizure type • EEG interictal expression • Anatomical substrate • Etiology • Age

ILAE 1981

Clinical seizure type | EEG sz type | EEG interictal expression

1. Partial (focal, local) seizures
Simple partial sz
- with motor signs
- with somatosensory symptoms
- with autonomic symptoms and signs
- with psychic symptoms

Complex partial sz
- start with SPS followed by impairment of consciousness
- with impairment of consciousness at onset

Partial sz evolving to 2^0 gen sz
- SPS → GTC
- CPS → GTC
- SPS → CPS → GTC

2. Generalized sz (convulsive and non-convulsive)
Absence, Myoclonic, Clonic, Tonic, Tonic-clonic, Atonic

3. Unclassified epileptic sz

4. Prolonged or repetitive seizure (status epilepticus)

ILAE 1989

1. Localization-related epilepsies and syndromes

1.1 Idiopathic
- benign childhood epilepsy with centro-temporal spike
- childhood epilepsy with occipital paroxysms
- primary reading epilepsy

1.2 Symptomatic e.g. TLE, FLE, PLE, OLE

1.3 Cryptogenic

ILAE 1989

2. Generalized epilepsies and syndromes

2.1 Idiopathic (with age-related onset, listed in order to age)
- Benign neonatal familial convulsions
- Benign neonatal convulsions
- Benign myoclonic epilepsy of infancy
- Childhood absence epilepsy (pyknolepsy)
- Juvenile absence epilepsy
- Juvenile myoclonic epilepsy
- Epilepsy w grand mal (GTCS) sz on awakening
- etc.

2.2 Cryptogenic or symptomatic (in order to age)
- West syndrome
- Lennox-Gastaut syndrome
- Epilepsy w myoclonic-astatic sz
- Epilepsy w myoclonic absences

ILAE 1989

2. Generalized epilepsies and syndromes

2.3 Symptomatic

2.3.1 Non specific etiology

- EME
- EIEE w supression burst
- other symptomatic generalised epilepsies not defined above

2.3.2 Specific syndromes/etiologies

- Cerebral malformation
- IBEM

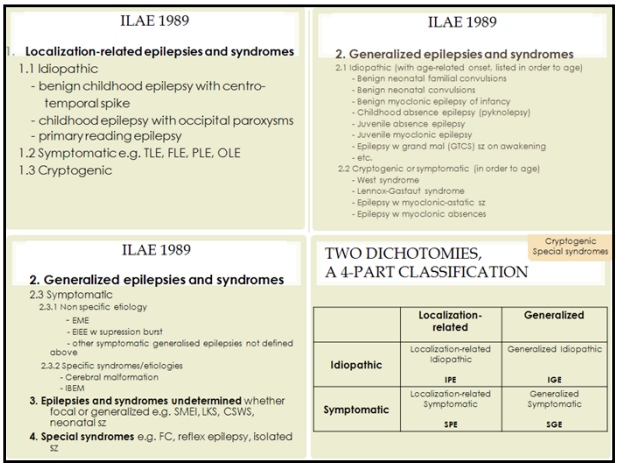
3. Epilepsies and syndromes undetermined whether focal or generalized e.g. SMEI, LKS, CSWS, neonatal sz

4. Special syndromes e.g. FC, reflex epilepsy, isolated sz

TWO DICHOTOMIES, A 4-PART CLASSIFICATION

Cryptogenic
Special syndromes

	Localization-related	**Generalized**
Idiopathic	Localization-related Idiopathic **IPE**	Generalized Idiopathic **IGE**
Symptomatic	Localization-related Symptomatic **SPE**	Generalized Symptomatic **SGE**



2001

Axis 1: Ictal phenomenology
Axis 2: Seizure type
Axis 3: Epileptic syndromes
Axis 4: Etiology
Axis 5: Impairment

2010

2005-2009

ILAE CLASSIFICATION WORKING GROUP

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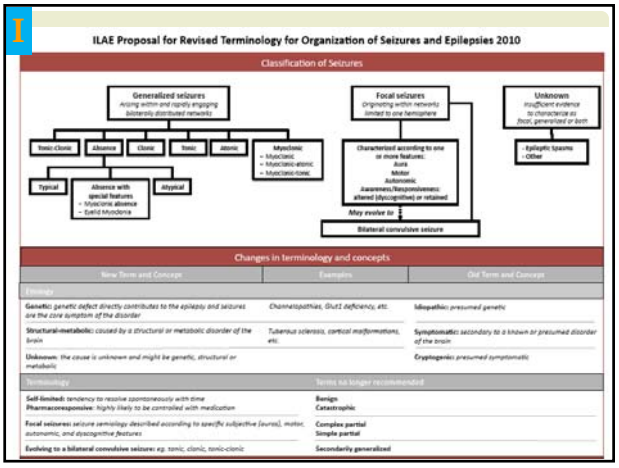


old New

Table 1. Comparison of major changes between the 1989 and 1981 Classification and Terminology and the newly proposed Terminology and Concepts (Commission 1981, 1989; Berg et al., 2010)

Old terminology and concepts	Recommended new terminology and concepts
Focal and generalized	
For seizures	
Focal (previously "partial"): the first clinical and electroencephalographic changes indicate initial activation of a system of neurons limited to a part of one cerebral hemisphere	Focal seizures are conceptualized as originating at some point within networks limited to one hemisphere
Generalized: the first clinical changes indicate initial involvement of both hemispheres	Generalized seizures are conceptualized as originating at some point within and rapidly engaging bilaterally distributed networks
For epilepsies	
Localization-related (focal, partial): epilepsies with focal seizures	These terms were abandoned as overarching categories for classifying epilepsies per se, as many syndromes include both seizure types; they may still apply in some but not all instances
Generalized: epilepsies with generalized seizures	

- The use of generalized and partial (focal) to refer to the underlying was abandoned
- But the terms were retained in reference to mode of seizure initiation and presentation

focal seizure should be described according to their manifestation

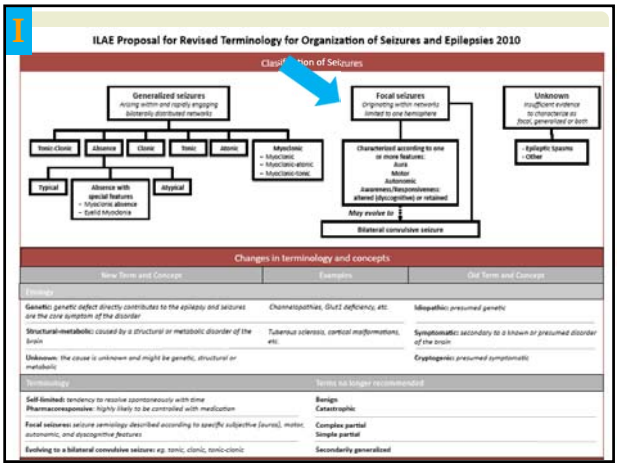
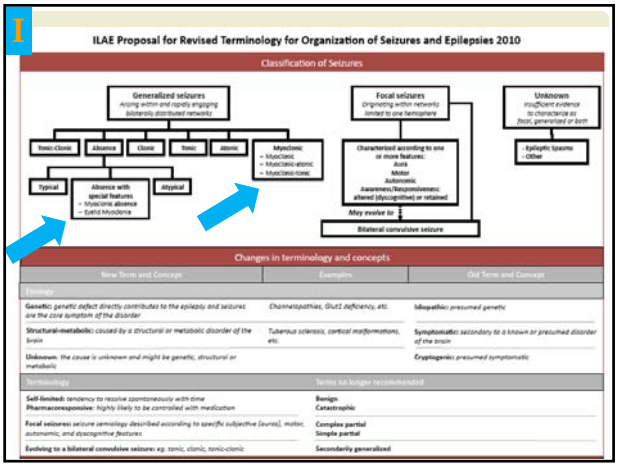


TABLE 1-4 Seizure Types and Terminology Used in the 1981 Classification of Seizures and Recommended in the 2010 Report[a,b]

Mode of Onset	1981 Seizure Types[c]	2010 Seizure Descriptions[d]
Focal	Simple partial	Without impairment of consciousness or awareness:
	With motor signs	With observable motor or autonomic components
	With sensory symptoms	
	With autonomic symptoms	
	With psychic symptoms (but no impaired consciousness)	Involving subjective sensory or psychic phenomena only, corresponding to the concept of an aura
	Complex partial	With impairment of consciousness or awareness. Dyscognitive is a term that has been proposed for this concept.[75]
	Consciousness impaired at onset	
	Simple partial onset followed by impairment of consciousness	
	Partial evolving to secondarily generalized seizure (tonic, clonic, or tonic-clonic)	Evolving to a bilateral, convulsive seizure (involving tonic, clonic, or tonic and clonic components).
	Simple evolving to generalized tonic-clonic	
	Complex evolving to generalized tonic-clonic (including those with simple partial onset)	
Generalized onset	Tonic-clonic	Tonic-clonic (in any combination)
	Myoclonic	Myoclonic
		Myoclonic-atonic
		Myoclonic-tonic
	Absence	Absence
	With various accompanying manifestations	Typical absence
	Atypical	Atypical absence
		With special features
		Eyelid myoclonia[e]
		Myoclonic absence
	Clonic	Clonic
	Tonic	Tonic
	Atonic (adiatic)	Atonic
Not clear	Anything that does not fit in above, eg, rhythmic eye movements, chewing, swimming movements	Epileptic spasms

Continuum 2013;19:571-597



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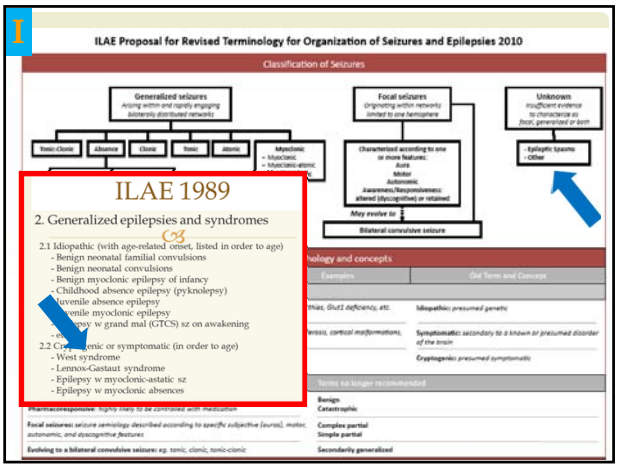
Generalized: epilepsies with generalized seizures	

Terminology	Terms no longer recommended
Self-limited: *tendency to resolve spontaneously with time*	**Benign**
Pharmacoresponsive: *highly likely to be controlled with medication*	**Catastrophic**
Focal seizures: *seizure semiology described according to specific subjective (auras), motor, autonomic, and dyscognitive features*	**Complex partial** **Simple partial**
Evolving to a bilateral convulsive seizure: *eg, tonic, clonic, tonic-clonic*	**Secondarily generalized**

focal seizure should be described according to their manifestation

I



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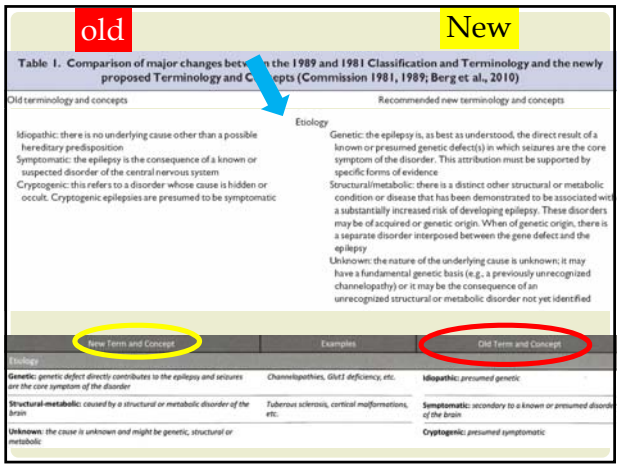

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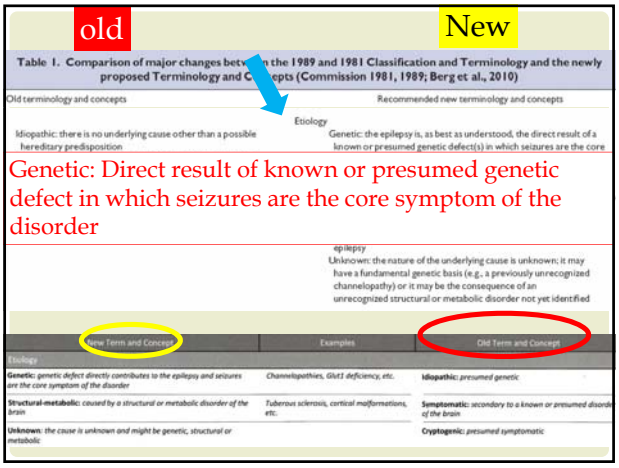

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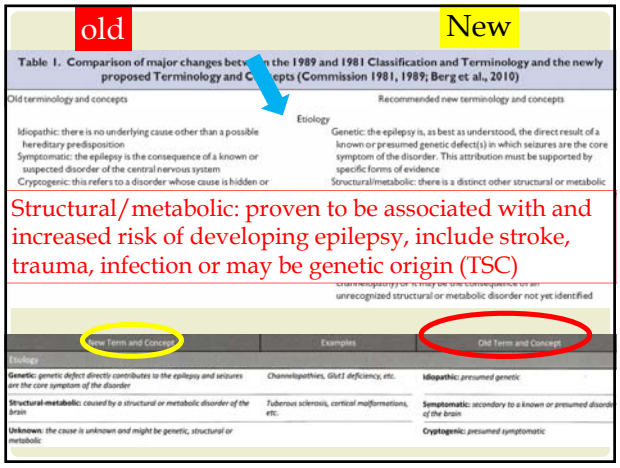

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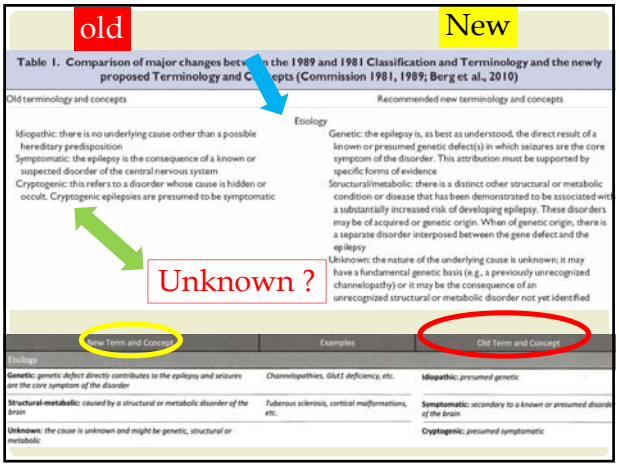

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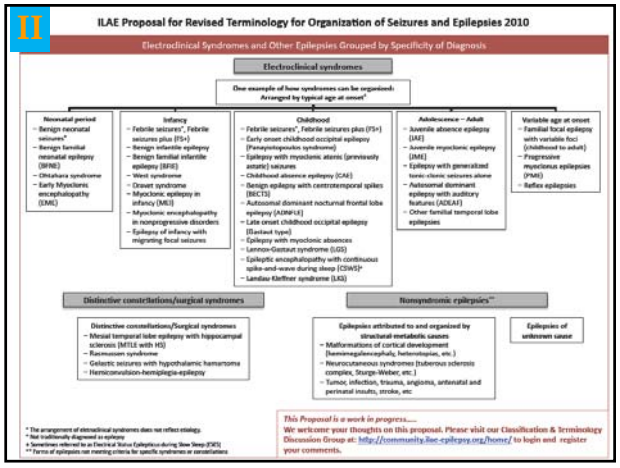
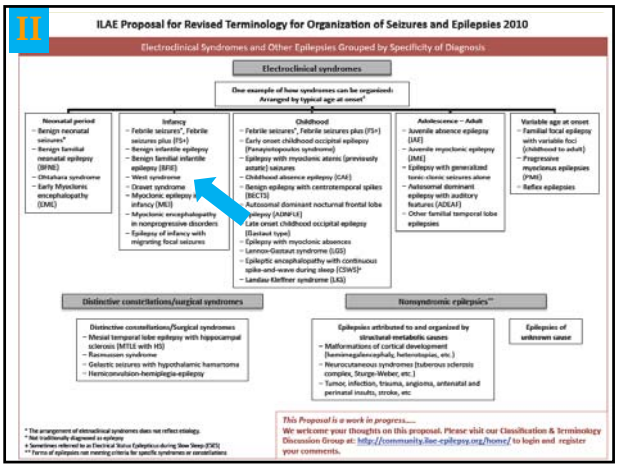


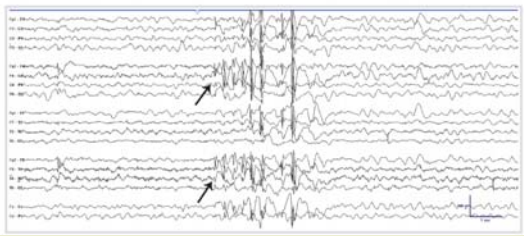


2010

- Classification system versus diagnosis
- 2010 entail little or no change in what health care providers do in daily practice
  (diagnose and treat individual patients)
- CAE : IGE (old)
  : generalized epilepsy, absence, genetic cause (new)

Case 1-1

A 3-year-old boy presented with persistent monthly seizures. Seizure onset was at 4 months old with recurrent hemiclonic seizures and status epilepticus, at times triggered by fever. Initial interictal EEG was significant for rare focal sharp-wave discharges in the right frontal region, and the original



Continuum 2013;19:571-597

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Causes of Epilepsy	Examples of Epilepsy Syndromes or Diseases
Genetic (single gene)*	
Channelopathies (*SCN1A; SCN1B; SCN2A; GABRG1; GABRG2; KCNQ2; KCNQ3; CHRNA4; CHRNB2; CHRNA2; KCNA1; CACNA1A*)	Dravet syndrome; generalized epilepsy with febrile seizures plus; benign familial neonatal convulsions; early myoclonic epilepsy; Ohtahara syndrome; autosomal dominant nocturnal frontal lobe epilepsy; juvenile myoclonic epilepsy; episodic ataxia types 1 and 2
Progressive myoclonic epilepsies (*CLN3; CLN5; CLN6; CLN8; CSTB; CTSD; EPM2A; MFSD8; NHLRC1; PPT1; PRICKLE1; TPP1; NEU1; DRPLA*)	Unverricht disease; neuronal ceroid lipofuscinoses; Lafora body disease; sialidosis; dentatorubral-pallidoluysian atrophy
Infantile developmental/genetic encephalopathies (*ALDH7A1; ARX; ATP6AP2; CDKL5; PCDH19; PNPO; SCN1A; SLC2A1; SLC19A2; SPTAN1; STXBP1; TSC1; TSC2; UBE3A; CNTNAP2; SCL9A6; NRXN1; TCF4; SYN1; FMR1; ZEB2; PNKP*)	Early myoclonic epilepsy; Ohtahara syndrome; West syndrome; pyridoxine-dependent epilepsy; glucose transporter type 1 deficiency syndrome; tuberous sclerosis complex; lissencephaly; early-onset absence epilepsy
Malformations of cortical development[b] (hamartomas, lissencephaly, periventricular nodular heterotopias, schizencephaly, double-cortex, heterotopias, cobblestone malformation, holoprosencephaly, polymicrogyria, etc)	Generally associated with nonspecific epilepsy presentation as well as with West and Lennox-Gastaut syndromes. Specific neurologic syndromes are associated with these malformations, eg, Walker-Warburg syndrome, Fukuyama congenital dystrophy
Neurometabolic/mitochondrial (*POLG; SURF1; ADSL*; mitochondrial DNA mutations; *GAMT; PSAP; MMACHC; OTC; PDHA1; PDHB; GALC*)	Generally associated with a nonspecific epilepsy presentation but cause specific neurologic syndromes or conditions, eg, Alper syndrome; Leigh syndrome; adenylosuccinate lyase deficiency; myoclonic epilepsy with ragged-red fibers; mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes; creatine deficiency syndrome; Gaucher disease; cobalamin C deficiency; ornithine transcarbamylase deficiency; pyruvate dehydrogenase deficiency; Krabbe disease
Other genetic (*LGI1*; trisomy 21)	Autosomal dominant epilepsy with auditory features (also known as autosomal dominant lateral temporal lobe epilepsy; Down syndrome; Ring chromosome 20
Neoplasms with known or suspected genetic contributions	Dysembryoplastic neuroepithelial tumor; hypothalamic hamartoma; glioma; gangliogliomas; meningioma

TABLE 1-8 Examples of Specific Genes First Associated With One Epilepsy Syndrome and Then Found to be Associated With Very Different Epilepsy Syndromes[a]

Gene (Protein Function)	Associated Electroclinical Syndromes	Brief Description of Syndrome
SCN1A (α-1 subunit of the neuronal voltage-gated sodium channel)	Dravet syndrome[27,28]	Onset <1 y old; multiple seizure types, often prolonged hemiconvulsions; progressive cognitive impairment; EEG evolves from normal to background slowing with admixed multifocal polyspike-wave discharges
	Epilepsy in females with mental retardation[29]	Onset <1 y old (often <6 mo old); focal seizures with prominent autonomic features (apnea, flushing, cyanosis); progressive cognitive impairment; EEG background slowing with admixed multifocal spike-wave discharges
	Generalized epilepsy with febrile seizures plus[30]	Onset in early childhood; may have febrile seizures initially, but continue to have fever-triggered seizures of all types after 6 y old; development may be normal, variable; EEG is normal or abnormal (generalized or multifocal)
SLC2A1 (glucose-transport protein 1)	Severe glucose transporter type 1 (*GLUT1*) deficiency syndrome[31]	Onset in infancy; epileptic encephalopathy with multiple seizure types; progressive cognitive decline; movement disorder; acquired microcephaly; EEG shows background slowing with generalized or multifocal spike-wave discharges
	Early-onset absence[32]	Onset <4 y old; refractory absence seizures; initially normal development, but may decline; EEG shows generalized spike-wave discharges
	Doose syndrome[33,34]	Onset in early childhood; multiple seizure types, but predominantly myoclonic and atonic seizures; development may be normal, variable; EEG background may evolve from normal to diffuse background slowing; generalized polyspike-wave discharges
	Nonsyndromic focal[35]	Epilepsies with predominantly focal electrographic and semiologic manifestations, the features of which do not correspond to any well-delineated electroclinical syndrome; such epilepsies are occasionally found in association with genetic errors that themselves are typically associated with very distinct electroclinical syndromes
KCNQ2 (neuronal potassium channel)	Benign familial neonatal epilepsy[36]	Onset at birth; multiple seizures types; development normal; interictal EEG normal
	KCNQ2 encephalopathy[37]	Onset at birth to first weeks/months; myoclonus or brief tonic seizures as an infant, but seizures usually well controlled by 3 y old; poor neurodevelopmental outcome; EEG background severely abnormal with suppression-burst during infancy and gradually evolves toward normal after several years

TEST

- A 25 year-old woman has two unprovoked seizures one year apart

Q: Epilepsy ? Old definition , New definition?
A:

TEST

A 65-year-old man had a left MCA stroke 6 weeks ago and now presented with un provoked seizure

Q: Epilepsy ? , Old definition /New definition
A:

Stroke has high risk (> 70%) of further sz

TEST

- A 6-year-old boy has had 2 seizures 3 days apart while playing a VDO game involving flash light. There have been no other seizure.
- EEG shows an abnormal photoparoxysmal response.

Q: Epilepsy ? Old definition , New definition

TEST

- A 22-year-old man had seizures with face twitching when falling asleep at ages 9,10,14 years; none since.
- EEG at age 9 years showed CT spikes.

Q: epilepsy ?
A:

Epilepsy is no longer present, 2013
Epilepsy is resolved, 2014

TEST

- A 40-year-old man had a focal seizure characterized by left hand twitching that progressed to a tonic-clonic seizure. This was his only seizure.
- MRI shows a probable transmantle dysplasia in the RF.
- EEG shows R F-T interictal spikes.

- Q: treat ?
- Q : epilepsy ?

TEST

- A 70-year-old woman had unprovoked seizure at ages 15 and 70. EEG, MRI and FHx are unremarkable.
- Q: epilepsy ? Old definition , New definition
- Q : treat ?
- Q: if two seizures have different causes ?

TEST

- An 85 year-old man had a focal sz at age 6 and another at age 8 years. EEG, MRI, blood tests and FHx were all unrevealing.
- He received AED from age 8-10.
- After off AED, no more seizure.

Q: Still epilepsy ?

TEST

- A 20-year-old man: 3 unobserved episodes in 6 months
- Sudden fear, difficulty talking, need to walk around
- Not aware of any memory loss during the episodes
- No other symptoms
- Routine EEG, MRI : normal
- Q: Epilepsy ? Old or New definition ?

Thank you for your time