Classification as a Barrier to Care
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Anne T. Berg, Ph.D.
Epilepsy Center
Children’s Memorial Hospital
Chicago, Il, USA
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Learning Objectives

• Understand the difference between diagnosis and classification and their relevance to epilepsy care
What is a classification and what should it do?

- A classification is a system for representing knowledge about items that are then placed within that system so as to reflect key characteristics.

- Teach (G. D. Jackson, 2011).
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Purpose of the International Classification of Seizures and Epilepsies

- “To provide a common international terminology and classification – a precondition for comparability of results in research and therapy and for meaningful exchange of ideas”
ILAE Classifications of Epilepsy and Seizures

- 1969 – Gastaut – Proposals - seizures & epilepsies
- 1970 – Gastaut – Classification - seizures
- 1970 – Merlis – Classification - epilepsies
- 1981 – Commission – Classification – seizures
- 1985 – Commission – Classification - epilepsies
- 1989 – Commission – Classification - epilepsies
- 1993 – Commission – epidemiological standards
- 2001 – Blume – Glossary of ictal semiology
- 2001 – Engel – Proposed diagnostic scheme
- 2005 – Fisher – Definition of seizure and epilepsy

All in Epilepsia
Purpose of the International Classification of Seizures and Epilepsies

- “To provide a common international terminology and classification – a precondition for comparability of results in research and therapy and for meaningful exchange of ideas”

- Largely for clinical (treatment) purposes

- Research into causes and mechanisms was not a dominant focus
Scientific advances since the 1950s and 1960s

- Genomic technology
- Molecular genetics
  - techniques and concepts
- Neuroimaging
  - structural and functional
- Neurophysiology
- Computational capabilities
- Therapeutic options
- ...
1989 Classification of the Epilepsies

1. Localization-related (partial)
   1.1 Idiopathic
   Specific syndromes
   1.2 Symptomatic
   Specific syndromes
   1.3 Cryptogenic
   Specific syndromes

2. Generalized
   2.1 Idiopathic
   Specific syndromes
   2.2 Cryptogenic/symptomatic
   Specific syndromes

2.3 Symptomatic
   Specific syndromes

3. Undetermined
   3.1 With both partial and generalized features
   Specific syndromes
   3.2 Without unequivocal partial or generalized features
   = “nonclassified”

Commission Report, Epilepsia 1989

*†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
Terms and Concepts

- Terminology:
  - Words should say what they mean, mean what they say
  - Based on relevant, useful, valid concepts
  - Use should be transparent

- Old terms are **barriers**:
  - Idiopathic-symptomatic-cryptogenic
  - Generalized epilepsy – focal epilepsy
  - Complex partial – simple partial
Terminology for etiology

- **Idiopathic** – “There is *no underlying cause* other than a possible hereditary predisposition. Idiopathic epilepsies are defined by age-related onset, clinical and electroencephalographic characteristics, and a *presumed genetic etiology*.”

- **Symptomatic** epilepsies and syndromes are considered the consequence of a *known or suspected* disorder of the central nervous system (CNS).

- **Cryptogenic** refers to a disorder whose cause is hidden or occult. Cryptogenic epilepsies are *presumed to be symptomatic*, but the etiology is not known.

  - Commission Report, Epilepsia, 1989
Say what you mean

- **Genetic**: the epilepsy is the direct result of a known or inferred genetic defect(s). Seizures are the core symptom of the disorder.
  - Requires knowing the mechanism
    - e.g. Channelopathies

- **Structural – Metabolic**: There is a *distinct other structural or metabolic condition or disease* present.
  - Provide precise identification of cause

- **Unknown**: The underlying cause is as yet unknown.
  - Could be genetic, structural, metabolic

  - Commission Report, Epilepsia 2010
“Idiopathic” & “Symptomatic”
Sloppy Connotations

- Idiopathic:
  - “Benign, easily treated”
  - **Instead: say what you mean**
    - Self-limited
      - The epilepsy often resolves on its own in time
    - Pharmacoresponsive
      - The seizures have a high likelihood of coming under complete control with AEDs

- Symptomatic
  - Bad outcome
    - Seizures
    - Cognitive-developmental
  - **Instead: Say what you mean**
    - Pharmacoresistant
    - Surgically remediable
    - Risk of developmental impairment
More barriers: Focal and Generalized Epilepsies

- Red herring - distraction
- Clinical relevance?
  - West & CAE are generalized
  - BECTS and gelastic seizures with hypothalamic hamartoma are focal

- Missed opportunities, inappropriate treatment
- Surgical implications:
  - Focal implied potentially surgical
    - Inappropriate use of surgery: Dravet, ADNFLE
  - Generalized implied not surgical
    - Failure to refer: West, LGS

- Separate manifestations from underlying process and cause
“Generalized” Seizure types

Tonic-clonic (in any combination)

Absence
  - Typical
  - Atypical
  - Absence with special features
    - Myoclonic absence
    - Eyelid myoclonia

Myoclonic
  - Myoclonic
  - Myoclonic atonic
  - Myoclonic tonic

Clonic
Tonic
Atonic
Terminology for Seizures

- **Focal Seizure Types**
  - Complex Partial
  - Simple Partial
  - Secondarily Generalized

Reduce array of highly diverse ictal events into 3 artificial, often arbitrary categories

- **Generalized Seizure Types**
  - Tonic-clonic (in any combination)

  - Absence
    - Typical
    - Atypical
    - Absence with special features
      - Myoclonic absence
      - Eyelid myoclonia

  - Myoclonic
    - Myoclonic
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  - Clonic
  - Tonic
  - Atonic

Spasms
Focal Seizures

Subjective (auras)

Objective

Autonomic (specific observations)

Dyscognitive (specific observations)

Motor

Elementary (specific observations)

Complex – automotor (specific observations)

Negative (specific observations)

Blume et al. Glossary of ictal semiology, Epilepsia 2001
Diagnoses versus Classification

Benign familial neonatal epilepsy (BFNE)
Early myoclonic encephalopathy (EME)
Ohtahara syndrome
Epilepsy of infancy with migrating focal seizures
West syndrome
Myoclonic epilepsy in infancy (MEI)
Benign familial infantile epilepsy
Dravet syndrome
Myoclonic encephalopathy in non progressive disorders
Febrile seizures plus (FS+)
Panayiotopoulos syndrome
Epilepsy with myoclonic atonic (seizures
Benign epilepsy with centrotemporal spikes
Autosomal-dominant nocturnal frontal lobe epilepsy

Late onset childhood occipital epilepsy
Lennox-Gastaut syndrome
Landau-Kleffner syndrome (LKS)
Childhood absence epilepsy (CAE)
Juvenile absence epilepsy (JAE)
Juvenile myoclonic epilepsy (JME)
Epilepsy with generalized tonic/clonic seizures alone
Progressive myoclonus epilepsies (PME)
Autosomal dominant epilepsy with auditory features
Familial focal epilepsy with variable foci
Reflex epilepsies
Mesial temporal lobe epilepsy with HS
Rasmussen syndrome
Gelastic seizures with hypothalamic hamartoma
Not all epilepsy diagnoses are equal:

- **Specific**
  - Electro-clinical syndrome, e.g. ...
    - Dravet
    - West
    - CAE
  - Surgical syndrome, e.g. ...
    - Rasmussen syndrome
    - Hypothalamic hamartoma w/gelastic seizures

- **Less specific:**
  - Nonsyndromic epilepsy secondary to specific cause, e.g.
    - TSC
    - FCD

- **Least specific:**
  - Nonsyndromic epilepsy of unknown cause
1989 Classification of the Epilepsies

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   1.1 Idiopathic
   Epilepsy diagnoses
   1.2 Symptomatic
   Epilepsy diagnoses
   1.3 Cryptogenic
   Epilepsy diagnoses

2. Generalized
   2.1 Idiopathic
   Epilepsy diagnoses
   2.2 Cryptogenic/symptomatic
   Epilepsy diagnoses

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   3.2 Without unequivocal partial or generalized features
   Epilepsy diagnoses"
Concerns and Complaints

- Most syndromes are very rare
  - True
  - But these syndromes inform care
- They are hard to recognize unless you are a specialist
  - True, experience is needed
  - But common ones are easily recognized
- Based on arbitrary criteria
  - True to an extent, in the past
  - Less so with genomic and imaging evidence
- Most epilepsies do not fit clear syndromic diagnoses
  - Also true, ~50% in children, 90% adults
  - But, they are important when they can be recognized
Poor man’s diagnosis of the Epilepsies:

1. Partialization-related
   1.1 Idiopathic
   1.2 Symptomatic
   1.3 Cryptogenic

2. Generalized
   2.1 Idiopathic
   2.2 Cryptogenic/symptomatic

2.3 Symptomatic
   Specific syndromes

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   = “unclassified”
Poor man’s diagnosis of the Epilepsies: A Barrier

- Give false sense of knowledge
- Discourages precision
- Encourages diagnostic errors
- Leads to
  - Poor care
  - Poor treatment
  - Poor outcomes
Ideally: a classification should…

- Teach the features that are essential about the epilepsies to be classified.
- Essential to ...
  - Diagnosis
  - Evaluation
  - Treatment
  - Long-term outcomes, counseling
- Organize information in a clear, accessible way.
- Teach and help physicians and others to diagnose and care for patients effectively
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Is a Classification essential for patient care?

- A dog is a dog is a dog
  - Animal, chordate, mammal, carnivore, canidae, canis..

- CAE
  - Idiopathic Generalized epilepsy

- or West
  - Generalized cryptogenic-symptomatic epilepsy
Oft repeated concerns of proponents of the “Poor Man’s Diagnosis”

- “Keep it simple for clinicians”
- The classification must be kept simple for students
- Make it relevant for practice in resource poor areas
A few broad strokes

- Simplified diagnostic and teaching approach
- Nonspecialist, teaching ...
  - Pediatrician
  - Internists
  - General neurologists
  - Nurses, APNs
  - Others
1) Babies are hard

Onset <2-3 years (~1/3 of pediatric epilepsy)

Evaluate by pediatric specialist

large number of rare genetic, structural, metabolic causes and syndromes

N.I.C.E. guidelines, UK

http://www.nice.org.uk/
2) Most, but not all, epilepsy requires imaging

Imaging guidelines
- *Gaillarde et al. Epilepsia 2009
- Fountain et al., Neurology 2011
  - *Exceptions are CAE, JAE, JME, BECTS (25% peds epil)

Be able to diagnose CAE, JAE, JME, BECTS

Important implications
- imaging
- selection of AEDs
- anticipatory counseling
3) Most generalized features outside of CAE, JAE, JME

Evaluate by epilepsy specialist

(a suggestion)
4) Unexplained neurological deficit at any age

Evaluate by team that can diagnosis and treat the underlying cause
- Imaging
- Genetic testing
- Metabolic
- EEG

Get as specific a diagnosis of cause possible
5) Development or worsening of neurological deficit, after onset of epilepsy

Evaluate by epilepsy or other appropriate specialist
6) Failure of first 2 AEDs

Referral to comprehensive center

- Definition of pharmacoresistant epilepsy
  - Kwan et al., Epilepsia 2000
- Referral guidelines for comprehensive evaluation
  - Cross et al. Epilepsia 2006
  - NAEC, Epilepsia 2010
Classification has been a barrier

- Don’t Classify!
- Diagnosis!

- Look to guidelines and reasonable recommendations.