North American Commission Symposium
Epilepsy Classification:
Hot Controversies in 2012

Symposium Co-Chairs:
Ingrid E Scheffer, MBBS, PhD, FRACP
The Florey Institute
University of Melbourne
Australia

and

Sheryl Haut, M.D.
Montefiore Medical Center
Bronx, NY

Tuesday, December 4, 2012
Convention Center – Ballroom 6A, Upper Level
8:30 am – 10:00 am
OVERVIEW
Classification of the epilepsies is a dynamic concept that continues to undergo reevaluation, especially in light of advances in structural and functional neuro-imaging, genetics and neuro-immunology. This symposium, sponsored by the International League Against Epilepsy, will focus on the newly updated organization of the epilepsies, exploring the emerging concept of diagnostic specificity and how this relates to clinical practice. Controversies that have arisen regarding the specific aspects of classification, namely structural, genetic and immune, will be presented.

LEARNER OUTCOMES
- Utilize the greater diagnostic specificity provided by the revised classification in managing patients and in doing research
- Utilize newly described genetic and immunologic testing in order to provide greater specificity in diagnosing epilepsy and in managing patients
- Utilize the revised classification to improve diagnostic specificity and coding accuracy for clinical epilepsy practice.

TARGET AUDIENCE
Basic: Those new to epilepsy treatment or whose background is limited, e.g., students, residents, general physicians, general neurologists and neurosurgeons, other professionals in epilepsy care, administrators.

Intermediate: Epilepsy fellows, epileptologists, epilepsy neurosurgeons “mid-level” providers with experience in epilepsy care (e.g., advanced practice nurses, nurses, physician assistants), neuropsychologists, psychiatrists, basic and translational researchers.

Advanced: Symposium will address highly technical or complex topics (e.g., neurophysiology, advanced imaging techniques, advanced treatment modalities, including surgery)

AGENDA
8:30 – 8:35 am Introduction and Overview
Sheryl Haut, M.D.

8:35 – 8:45 am Update on the new Organization: Where Have the Modifications Taken Us?
Ingrid E. Scheffer, Ph.D.

8:45 – 9:00 am Diagnostic Specificity: Applying This Concept to Every Patient
J. Helen Cross, M.D., Ph.D.

9:00 – 9:10 am Controversies: Genetic: How Do I Tell the Patient?
Sameer Zuberi, MD

9:10 – 9:25 am Controversies: Genetic: Structural: Genetic or Acquired?
James Barkovich

9:25 – 9:40 am Immune: Which Patients Should Be Tested?
Christian Bien, M.D.

9:40 – 9:55 am Coding: Will This Make a Difference to My Practice?
Donna C. Bergen, M.D.
9:55 – 10:00 am Conclusions
Ingrid E. Scheffer, Ph.D.

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International Credits: The American Medical Association has determined that non-U.S. licensed physicians who participate in this CME activity are eligible for AMA PRA Category 1 Credit™.

ABPN Core Competencies
The American Board of Psychiatry and Neurology has reviewed the North American Commission and has approved this program as part of a comprehensive lifelong learning program, which is mandated by the ABMS as a necessary component of maintenance of certification.

Core Competencies: Medical Knowledge, System-Based Practice, and Practice-Based Learning and Improvement

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FACULTY / PLANNER BIO AND DISCLOSURES

Ingrid Scheffer, M.B.B.S., Ph.D., FRACP (Co-Chair)
Ingrid Scheffer is a paediatric epileptologist and Senior Principal Research Fellow at the Florey Institute. She holds a Chair at the University of Melbourne, Austin Health and Royal Children's Hospital, Melbourne, Australia. Her major interests are epilepsy syndrome classification and the genetics of the epilepsies. In recent years, she has focused on the epileptic encephalopathies and all genetic forms of epilepsy. She is currently the chair of the ILAE Commission for Classification and Terminology.

Ingrid Scheffer, M.B.B.S., Ph.D., has nothing to disclose.

Sheryl Haut, M.D. (Co-Chair)
Dr. Sheryl Haut is Director of the Montefiore-Einstein Adult Epilepsy Program and Director of Neurology Residency Training at Albert Einstein College of Medicine. She is also the Chair of the North American Commission of the International League Against Epilepsy. Her research interests include: the temporal distribution of seizures, with emphasis on seizure clustering; seizure prediction and pre-emption; and alternative therapies for epilepsy. Dr. Haut has a Masters in Clinical Research Methods, and completed a K23 career development award from the NIH. She maintains an active adult epilepsy practice at Montefiore Medical Center, Bronx NY.

Sheryl Haut, M.D. discloses receiving support as Consulting/Advisory Board Activity from MAP Pharmaceuticals; Vivus; Neuronex; Upsher Smith.

James Barkovich, M.D.
Dr. Barkovich is Chief of Pediatric Neuroradiology at UC San Francisco. He is a neuroradiologist whose clinical specialties are pediatric neuroradiology and epilepsy imaging. Dr. Barkovich’s research interests include normal brain development and disruptions of normal developmental processes including genetic causes, disruptions with resultant malformations of the brain, and perinatal/neonatal brain injury. In addition, he helps to develop and use novel imaging techniques to detect developmental and acquired causes of epilepsy and abnormal neurodevelopment.

James Barkovich, M.D. has nothing to disclose.

Donna Bergen, M.D.
I am Professor of Neurological Sciences at Rush University, working mainly in clinical epileptology. I have a special interest in issues of provision of care, and in drug development. For the past several years I have served on the World Health Organisation’s Task Force Advisory Group in Neurology, for the revision of the ICD-10 codes.
Donna Bergen, M.D. discloses receiving support as Research Funding from For Profit Commercial Sources/Principle Investigator from Medtronic, therapeutic trial.

Christian Bien, M.D.
Dr. Christian G. Bien is (since Januar 2011) Clinical Director of Krankenhaus Mara, Epilepsy Center Bethel, Bielefeld/Germany. He obtained his Medical Degree from the Free University of Berlin/Germany and completed his neurology training at the Medical Center of the University of Bonn/Germany. His main fields of clinical and research activities are presurgical assessment of pharmaco-resistant epilepsy patients chronic immune-mediated brain disorders as a cause of seizure disorders. He runs a lab for determination of antineural antibodies at his hospital.

Christian Bien, M.D. discloses receiving support as Speakers Bureau Member (supported by for-profit entities) from Eisai, UCB, GlaxoSmithKline and Desitin (all Germany); as Consulting/Advisory Board Activity from Eisai and UCB, both Germany

J. Helen Cross, M.D., ChB, Ph.D.
Professor Helen Cross is The Prince of Wales’s Chair of Childhood Epilepsy and Honorary Consultant in Paediatric Neurology at UCL-Institute of Child Health, Great Ormond Street Hospital for Children NHS Trust, London and Young Epilepsy, Lingfield, UK. She currently sits on the ILAE Commission for European Affairs, and has recently been elected as ILAE Secretary General (from 2013). In 2007 she was awarded an Ambassador for Epilepsy Award by the ILAE. Her research interests include aetiology of the epilepsies, as well as the role of early surgical intervention and other new treatments in childhood epilepsy.

J. Helen Cross, M.D., ChB, Ph.D. discloses receiving support as Consulting/Advisory Board Activity from Advisory Board for Eisai and Viropharma, honoraria paid to department; as Honoraria from Commercial Sources from Viropharma; paid to department.

Sameer Zuberi, M.D.
Sameer M Zuberi is Consultant Paediatric Neurologist at the Royal Hospital for Sick Children, Glasgow, UK. He is Clinical Lead of the Glasgow Epilepsy Genetics Service and Paediatric Neurosciences Research Group. He is Education Officer of the ILAE Commission for Classification and sits on the Board of the European Paediatric Neurology Society. His clinical and research interests include epilepsy genetics (particularly impact on clinical care), differential diagnosis and the channelopathies.

Sameer Zuberi, M.D. has nothing to disclose.

Paul Levisohn (Medical Content Specialist)
Dr. Levisohn is Associate Professor of Pediatrics and Neurology at the University of Colorado School of Medicine and Children’s Hospital Colorado. He is former medical director of the Epilepsy Monitoring Unit at The Children’s Hospital. He has served as chair of the AES Practice Committee, is co-chair of the advisory committee for the National Center for Project Access at the Epilepsy Foundation and is a member of the EF Professional Advisory Board. He currently serves as consultant to AES on medical content of AES continuing medical education activities.

Paul Levisohn, M.D. has nothing to disclose.

Ajay Gupta, MD (Liaison Reviewer)
Ajay Gupta, M.D., is Professional Staff in the Epilepsy Center/Neurological Institute at The Cleveland Clinic Foundation. He is Associate Professor at The Cleveland Clinic Lerner College of Medicine, Case Western Reserve University. He is also the founder director of multidisciplinary Tuberous Sclerosis
Program at the Cleveland Clinic. Dr. Gupta is an expert in the field of childhood and adolescent epilepsy with emphasis on epilepsy surgery evaluation and intra-operative monitoring. He has authored more than 75 original research articles and review papers in the peer-reviewed international journals.

Ajay Gupta, M.D. discloses receiving support as Salary from Commercial Sources generating W-2 from Cleveland Clinic; as Speakers Bureau Member (supported by for-profit entities) from Lundbeck Inc.

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Opinions expressed with regard to unapproved uses of products are solely those of the faculty and are not endorsed by the American Epilepsy Society or any manufacturers of pharmaceuticals.

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To help support this process, AES members who want CME will be asked to pay $35 before January 18 and $50 between January 19 and February 28. Non-AES attendees who want CME will be asked to pay $50 before January 18 and $75 between January 19 and February 28.

The online Evaluator will be left open through February 28, 2013. You must complete the evaluations and credit tracking by that date.

By completing this information online, attendees greatly assist the Council on Education and Annual Meeting Committee with important needs assessment data whereby the AES can further plan and address educational gaps to meet the needs of our learners.

A meeting attendance certificate will be available for international meeting attendees at the registration desk.

SYLLABUS
Syllabi for the educational symposia are available to print in the AES Virtual Tote Bag. Paper handouts will not be provided on site.
Epilepsy Classification: Hot Controversies in 2012
December 4th, 2012
Ingrid Scheffer, Ph.D and Sheryl Haut, M.D.
Symposium Co-Chairs
North American Commission of the International League Against Epilepsy Symposium 2012

Learning Objectives
1. Participants will become familiar with the revised classification system for epilepsy, which will lead to greater diagnostic specificity for epilepsy treatment and research
2. Participants will become more aware of the role of genetic and immunologic testing in epilepsy
3. Improvement in coding accuracy for clinical epilepsy practice.

ARS Question #1: What is your familiarity with the new ILAE Organization of the Epilepsies?
1. I am aware of the reports and have integrated changes into my clinical terminology
2. I am aware of the changes in classification but have not yet utilized them
3. I am not aware of the specifics of the new classification system

ARS Question #2: How have electroclinical syndromes changed in the new Organization of the Epilepsies?
1. They are a subgroup of the new etiological groups
2. They are considered a subgroup of genetic epilepsies
3. They are changed by the new concepts for focal seizures
4. Not at all
5. There are fewer syndromes

Disclosure

Dr. Haut
Acorda
Consultant

Vivus
Consultant

Upsher Smith
Consultant

Neuronex
Consultant

Dr. Scheffer
Nothing to disclose

Schedule
- Introduction—Sheryl Haut, M.D.
- Update on the new Organization: Where Have the Modifications Taken Us? Ingrid E. Scheffer, M.B.B.S., Ph.D.
- Diagnostic Specificity: Applying This Concept to Every Patient - J. Helen Cross, M.B.Ch.B., Ph.D.
- Controversies
  - Genetic: How Do I Tell the Patient? Sameer Zuberi, M.B.Ch.B., M.D.
  - Structural: Genetic or Acquired? James Barkovich MD
- Immune: Which Patients Should Be Tested? Christian Bien, M.D.
- Coding: Will This Make a Difference to My Practice? Donna C. Bergen, M.D.
- Conclusions - Ingrid E. Scheffer, M.B.B.S., Ph.D.
- Discussion
Update on the new Organization: Where have the modifications taken us?

Ingrid E Scheffer, MBBS PhD FRACP
Chair, ILAE Commission for Classification and Terminology
The Florey Institute, University of Melbourne, Australia

Disclosure

Name of Commercial Interest
None
Type of Financial Relationship
None

Impact on Clinical Care and Practice

• Primary clinical tool in daily practice
• Affects every patient we see
• Major impact on terminology for seizures
• Major impact on considering etiology of epilepsy

Learning Objectives

• To learn about the new Organization
• To understand how to use the new Organization

Purpose of the International Classification of Seizures and Epilepsies

• To provide a common international terminology and classification
• Largely for clinical (treatment) purposes
• Purpose of classification: to organize items according to their fundamental relationships

Refinements to the Organization

• We have listened to your valuable feedback!
• “Reinstated” focal and generalized epilepsies as useful diagnostic entities where they work
• Modified the organization to reflect emerging etiological subgroups
• Aim to reflect current understanding

SPECIAL REPORT


*Anita T. Berg, †Samuel F. Berkovic, ‡Martin Brodie, †Jeffrey Buchhalter, ‡M Helen Cross, †Walter van Bogaert, ‡Jennifer Engel, ‡Jacqueline French, ††Taryn A. Glazeon, ‡‡Gary W. Mathieson, ‡‡‡Salman R. Mishal, ‡Douglas Nordli, †††Porfiro Pineda, and ‡Ingrid E. Scheffer
**Concepts**

- Seizures
- Syndromes
- Etiologies

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**Focal seizures**

*Blume et al Epilepsia 2001*

- Previous term: simple partial
  - No impairment of consciousness or awareness
  - Motor or autonomic components eg. focal clonic
  - Subjective sensory or psychic features -> Aura
- Previous term: complex partial
  - Altered cognition -> Dyscognitive
- Previous term: secondarily generalized
  - Evolving to bilateral, convulsive seizure
  - With tonic, clonic or tonic and clonic components

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**Generalized seizures**

Tonic-clonic (in any combination)

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

- Myoclonic
  - Myoclonic
  - Myoclonic atonic
  - Myoclonic tonic

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Seizure types thought to occur within and result from rapid engagement of bilaterally distributed systems

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**Epilepsy syndromes**

- Unchanged!
- A diagnosis can be made as previously e.g.
  - Lennox-Gastaut syndrome
  - Childhood Absence Epilepsy
- A diagnosis is **not** the same as a classification
Etiology

- Genetic
- Structural
- Metabolic
- Immune
- Unknown

- Use terms that mean what they say!
- Replace old fashioned terms: idiopathic, symptomatic, cryptogenic

Genetic

- **Concept:**
  - Epilepsy is the direct result of a known or inferred genetic defect
  - Seizures are the core symptom of the disorder
- **Evidence**
  - appropriately designed family studies or
  - replicated molecular genetic studies
- Genetic does *not* exclude the possibility of environmental factors contributing

Structural

- **Concept:**
  - Epilepsy is the result of a distinct other structural condition or disease
    - eg. tuberous sclerosis
- **Evidence:**
  - Must have a substantially increased risk of developing epilepsy with the condition

Metabolic

- **Concept:**
  - Epilepsy is the result of a metabolic condition or disease with widespread manifestations
    - eg. aminoacidopathies
    - pyridoxine-dependent seizures
- **Evidence:**
  - Must have a substantially increased risk of developing epilepsy with the metabolic condition

Immune

- **Concept:**
  - Epilepsy is the result of autoimmune mediated central nervous system inflammation
    - eg. autoimmune encephalitides
    - anti-NMDA encephalitis
    - limbic encephalitis
- **Evidence:**
  - Must have a substantially increased risk of developing epilepsy with the immune condition

Unknown

- **Concept:**
  - The underlying cause is unknown
Diagnostic specificity

- Electroclinical syndromes
- Epilepsies due to a known cause may not be localizing
- Structural eg. Focal cortical dysplasia
- Metabolic eg. GLUT1 deficiency
- Also applies to Genetic and Immune epilepsies
- Constellations or Associations
- Related concepts – eg TLE with hippocampal sclerosis
- May carry surgical implications
- Unknown

Refinement of the Organization of the Epilepsies

- Changes in response to feedback - more “user friendly”
- Changes to seizure concepts well accepted
- Changes to seizure terminology being implemented
- Etiological subgroups now separated & immune added
- Flexible – you can organize it how you wish
- Must remain a dynamic and evolving classification
- Future – scientifically based classification based on biological mechanisms
Diagnosis Specificity: Applying This Concept to Every Patient

J Helen Cross
UCL-Institute of Child Health, Great Ormond Street Hospital for NHS Foundation Trust, London, & Young Epilepsy, Lingfield, UK.

Disclosure

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Learning Objectives

• To recognize how the classification can work in day to day clinical practice
• To demonstrate how diagnostic specificity may be improved

How does it work?

• Electroclinical syndrome diagnosis (organised by age of onset)
• Non syndromic epilepsy (by description) associated with specific aetiology
• Non syndromic epilepsy (by description) of unknown cause

Case 1

• Full-term normal delivery
• First seizure age 4 months, prolonged right sided generalised tonic-clonic seizures (GTCS)
• Further febrile seizure age 5 months, prolonged
• Is it epilepsy?
  – Complex febrile seizures

Case 1

• Treated with sodium valproate
• SCN1A mutation positive
• At 13m, presented with prolonged GTC seizures requiring ITU admission
• Increasing concern about her gait – unsteady
• Ultimately focal dyscognitive seizures +/- bilateral convulsive seizures, myoclonic jerks
• Up to 6 seizures per day for 3 days, with 1-2 days seizure-free
• Myoclonus daily
• Evidence of language delay
**Syndrome diagnosis?**

**2001**
- Focal or generalised?
- Idiopathic or symptomatic?
- How does this move us forward?

**2010**
- Dravet syndrome
- Genetic aetiology
- Prognosis
- Treatment options
- Genetic counselling

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**Case 2**

- Seizure onset 12m, ‘GTC’
- 8 hours post whooping cough vaccine
- Development multiple seizure types
- GTC, clonic, dyscognitive, myoclonic, SE

Now age 60 yrs
- Continued seizures
- Severe learning difficulties
- No speech
- PEG, wheelchair bound

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**Syndrome diagnosis?**

**2001**
- Focal or generalised?
- Idiopathic or symptomatic?
- Dravet syndrome?
- How does this move us forward?

**2010**
- Dravet syndrome
- Genetic evaluation
  - SCN1A positive
- Change in treatment
  - Spoken words

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**Case 4**

- Girl, emergency CS for poor heart rate
- Flat at birth, but recovered and sent to postnatal ward
- Seizure ‘eye rolling, shrill cry, abnormal positioning both arms’
- Limited response to phenobarbitone
- Normal MRI, metabolic evaluation negative at 6 weeks

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**Case 4**

- Age 5 months, episodes of left sided stiffening with eye deviation to left, and right sided stiffening with eye deviation to right
- Escalation in seizure frequency
- EEG ‘slow background, discharges over both hemispheres – 2 seizures recorded, asymmetric tonic & clonic’
- Age 4 years, infrequent GTC seizures, myoclonic jerks, dyskinesia upper limbs, profound neurodevelopmental delay
Syndrome diagnosis?

2001
• Focal or generalised?
• Idiopathic or symptomatic?
• How does this move us forward?

2010
• Epilepsy characterised by asymmetric tonic seizures, occurring in clusters, with movement disorder, of unknown aetiology
• Genetics 2012: KCNQ2 mutation

Impact on Clinical Care and Practice

• The new organisation helps to define the epilepsy for what it is
• With common terminology, phenotypes can be accurately described and aetiology more likely to be determined
• Accurate diagnosis enables optimal management and prognostic information for families – even if unknown
**Controversies**

**Genetic: How do I tell the patient?**

December 4, 2012

Dr Sameer M Zuberi MB ChB, MD, FRCP, FRCPCH
Paediatric Neurologist
Royal Hospital for Sick Children
Glasgow, UK

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**Disclosure**

Waterloo Foundation
Dravet Syndrome UK
Muir Maxwell Trust

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**Learning Objectives**

- Why is the term “genetic” replacing “idiopathic” for the genetic generalised epilepsies
- How do you explain complex inheritance in the epilepsies and de novo genetic epilepsies to patients and families
- What are the benefits and risks of genetic knowledge & genetic testing for the family
- How thinking about a genetic aetiology can improve your practice

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**Genetic**

The aetiology is deemed genetic where genetic factors play a major role in the causation of the individual’s epilepsy.

The concept of genetic relates to where the epilepsy is, to the best of our knowledge, the direct result of a known or presumed genetic defect and where seizures are the core symptom of the disorder.

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**Genetic epilepsies: How do I tell the patient?**

- A teenager with juvenile myoclonic epilepsy (JME) with or without a family history of generalised epilepsies
- The parents of a child with Dravet syndrome

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**The teenager with JME**

- A genetic generalised epilepsy (previously an idiopathic generalised epilepsy)
- How do you explain genetic when there is no family history?
  - Complex inheritance does not require a complex explanation
  - Most people have a concept of genes and inheritance
  - We all get copies of genes from our mother and from our father
  - It takes a particular combination of a few genes, some from mum, some from dad that aren’t working completely normally to cause your epilepsy
  - We don’t know what all these genes are yet and for most people we don’t have a genetic test we can do.
- Why wasn’t I grow out of my epilepsy but my cousin (with childhood absence epilepsy) did?
The parents of a child with Dravet syndrome
• How can it be genetic when there is no family history?
• If it is genetic is it my fault?
• Did I do something to cause the genetic mutation?

• Explaining what a genetic mutation / genetic variant is
  - Every time a human cell divides a sequence of 3 billion DNA units (nucleotides) needs to be replicated. Sometimes mistakes occur in copying the code
  - These variations / mutations are essential to allow evolution and change in all species.
  - Sometimes these variations occur by chance in important genes and can lead to genetic conditions

What are the benefits of identifying a genetic mutation [1]?
• Genetic testing may allow a diagnosis to be made earlier
• Genetic testing may guide treatment – focus medication choice & withdrawal
• Genetic testing may prevent additional investigations
• A clear genetic diagnosis improves access to therapies / community support

1. The clinical utility of an SCN1A genetic diagnosis in infantile-onset epilepsy
Brunkeus et al. Developmental Medicine & Child Neurology (in press)

Parent / carers views on genetic testing

Physicians views on genetic testing

Impact on Clinical Care and Practice
• Thinking genetics will focus the physician on defining an aetiology.
• Genetic testing has proven clinical utility
• Genetic testing, including panels of multiple genes, will become standard clinical practice
  - Clinicians must partner lab scientists in interpreting results
  - Genetic counseling must be available to individuals and families

sameer.zuberi@nhs.net
Structural: Genetic or Acquired?
Dec 4, 2012
A. James Barkovich, MD
University of California, San Francisco

Learning Objectives

• Learn MRI characteristics for “structural” causes of epilepsy.

Genetic/Structural/Metabolic Causes

• Genetic
  – Sodium/Potassium/NMDA receptor mutations
  – Many metabolic disorders
  – Many malformations

• Structural
  – Genetic malformations (hemimegalencephaly, cobblestone cortex, heterotopia, some PMG, some FCDs, etc)
  – Acquired malformations (infection, trauma, ischemia, seizures)

• Metabolic
  – Can cause primary (PMG in peroxisomal disorders) or secondary (e.g., from hyperammonemia) structural abnormalities

Structural Abnormalities associated with Epilepsy

• Hippocampal dysplasia or atrophy
• Cortical dysgenesis
  – Pachygria, polymicrogyria, FCD2
  – “Blurring” of cortical-white matter junction (may be 2” to immaturity)
  – Irregular cortical infolding
• Cortical atrophy (thinning)
  – Metabolic (e.g., NCL)
  – From prior infection, ischemia, injury (some of these are called FCD1)

Sensitivity of MRI in detecting Structural Lesion varies with:

– Age of baby at time of scan (FCD difficult to detect 5-18 months of age)
– Scanner (magnetic field and gradient) strength
– Sequences obtained
– Section thickness (thin with reformats is best)
– Signal to noise
– Expertise of interpreter (“You see what you look for, you look for what you know”)

– Inadequate MRIs must be repeated (often with anesthesia)
G-W blurring due to incomplete myelination. Try IR or wait until 24-30 months.

Focal Polymicrogyria: 3 mo with seizures

High resolution to distinguish PMG from Pachygyria. Currently MRI cannot dx genetic PMG from acquired

10 yo with refractory Epilepsy G-W Blurring
Dx: HME

22 year old woman
Mature PMG

5 yo girl
IQ ~50
Normal neuro exam
Epilepsy (gen) x 1 yr
Reelin pathway defect: Pachygyria
Band Heterotopia due to DCX mutations

Typical

Mild

5 month old with seizures 2nd birth injury

12 yo with refractory sz from left frontal FCD I

16 mo with Refractory Rt Frontal Seizures
Absent subcortical Myelin, reduced FDG uptake.
Dx: FCD I

9 yo with refractory epilepsy localized to right parietal lobe
Dx: FCD Ila Blurring of GWJ

FCD Iib Transmantle Sign Specific MRI sign
Frontal Lobe: FCD2a

Magnetic Source Imaging (MSI)

MEG interictal spike foci
coregistered with axial SPGR images

10 year old boy with partial complex epilepsy
FCD IIIa (FCD and MTS)

3 year old girl with Late Infantile NCL

Adjuncts to MRI for Epilepsy Imaging

- FDG Positron Emission Tomography (PET)
- Magnetoencephalography (MEG, called MSI when merged with MRI)
- MRI with computerized morphometric analyses
- fMRI
- Proton MR Spectroscopy (for metabolic causes)
Impact on Clinical Care and Practice

- Using correct imaging approaches/tools aids in establishing diagnosis
- Establishing correct diagnosis of structural lesion as cause of epilepsy helps in decisions on treatments
Learning Objectives

• By the end of this lesson, you should be able to identify epilepsy patients in which testing for anti-neural autoantibodies promises a favorable balance between positive and negative results.

Immune-mediated epilepsy: Which Patients Should Be Tested?

December 04, 2012

Christian G. Bien,
Epilepsy Center Bethel, Germany

Disclosure

Service on scientific advisory boards of UCB, Eisai.
Industry-funded travel with support of Eisai, UCB and Desitin.
Honoraria for educational speaking engagements from Eisai, UCB, GlaxoSmithKline, Desitin, Grifols.

Dr. Bien’s employer, Krankenhaus Mara, runs a laboratory for the detection of anti-neural autoantibodies.

Immune-mediated epilepsy - Tentative definition -

Brain disorder with recurrent seizures\(^1\), directly\(^2\) or indirectly\(^3\) caused by elements of the adaptive immune system (antibodies, T cells).
Immunotherapy may improve the condition.

\(^1\)Seizures are not necessarily the only symptom.
\(^2\)E.g., antibodies modify synaptic transmission in an epileptogenic manner
\(^3\)E.g., cytotoxic T cells destroy brain cells; the resulting scar gives rise to seizures

Immune-mediated epilepsy - Overview of autoantigens -

- Intracellular antigen
- Surface antigen

*Neuropil antibodies*
Immune-mediated epilepsy
- When should antibody testing be done?
- Syndrome:
  - Limbic encephalitis
  - Faciobrachial dystonic seizures
  - Encephalopathy
- Patient and history:
  - Young females
  - Other autoimmune conditions
- Seizure types and patterns:
  - Unexplained new onset epilepsy in adult life
  - Onset with status or very high seizure frequency
  - Pilocort seizures
- Paraclinical findings:
  - EEG: “extreme delta brush”
  - CSF: cell count 1 or unmatched oligoclonal bands
  - MRI: encephalitic lesions
  - Histopathology: “chronic encephalitis”

Immune-mediated epilepsy
- Case 1 -

Video will be shown

Immune-mediated epilepsy
- Case 1: female, 66 yrs -

Immune-mediated epilepsy
- Case 1: female 66 yrs -

*Syndrome:*
- Limbic encephalitis
- Faciobrachial dystonic seizures
- Encephalopathy
- Patient and history:
  - Young females
  - Other autoimmune conditions
- Seizure types and patterns:
  - Unexplained new onset epilepsy in adult life
  - Onset with status or very high seizure frequency
  - Pilocort seizures
- Paraclinical findings:
  - EEG: “extreme delta brush”
  - CSF: cell count 1 or unmatched oligoclonal bands
  - MRI: encephalitic lesion
  - Histopathology: “chronic encephalitis”

Immune-mediated epilepsy
- Case 2: 24 yrs -

Disease onset:

Within a fortnight ...
- Seizures (tonic-clonic? frontal lobe?)
- Apraxia
- Disorientation
- Aphasia
- Aggression
- Compulsory treatment in psychiatric hospital
**Immune-mediated epilepsy**

- **Case 2:** ♀ 24 yrs – Video -

  - Video will be shown

- **Case 2:** ♀ 24 yrs: EEG-

  - "Extreme delta brush" – NMDA receptor antibodies

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**Immune-mediated epilepsy**

- **Case 2:** ♀ 24 yrs -

  - "Syndrome":
    - Limbic encephalitis
    - Faciobrachial dystonic seizures
    - Encephalopathy
  - **Patient and history:**
    - Young females
    - Other autoimmune conditions
  - **Seizure types and patterns:**
    - Unexplained new onset epilepsy in adult life
    - Onset with status or very high seizure frequency
    - Pilocytic seizures
  - **Paraclinical findings:**
    - EEG: "extreme delta brush"
    - CSF: cell count 1 or unmatched oligoclonal bands
  - After 2 mo of immuno-tx: Improvement from mRS 5→3

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**Immune-mediated epilepsy**

- **Case 3: Faciobrachial dystonic seizures**

  - Video will be shown

  - LGI1 abs, sz-free 2 days after start of steroids

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**Impact on Clinical Care and Practice**

Limbic encephalitis, faciobrachial dystonic seizures, seizures in the context of encephalopathy, and other features suggest autoimmune epilepsy.

They should prompt antibody testing and immunotherapy.
Coding ICD-10: What It Means to Practice
Dec 4 2012
Donna Bergen MD
Professor of Neurological Sciences
Rush University Medical Center

Learning Objectives

• To apply the new ICD-10 codes for seizures and epilepsy to patient encounters
• To relate the ICD-10 codes to the proposed ILAE epilepsy classification

ICD-9: seizure codes

780.32 Complex febrile convulsions
   Includes: febrile seizure
   Atypical
   Complex
   Complicated

780.39 Other convulsions
   Includes: Convulsive disorder NOS
   Fits NOS
   Recurrent convulsions NOS
   Seizure NOS
   Seizures NOS

ICD-9: stray locations

333.2 Myoclonus
   Includes: progressive myoclonic epilepsy
   Unverricht-Lundborg disease

649.4 Epilepsy complicating pregnancy, childbirth, or the puerperium

Disclosure

Name of Commercial Interest: Medtronic
Type of Financial Relationship: Clinical trial
ICD-9: modifiers

345.40 Localization-related (focal) (partial) epilepsy and epileptic syndromes with complex partial seizures, not intractable

345.41 Localization-related (focal) (partial) epilepsy and epileptic syndromes with complex partial seizures, intractable

ICD-10

Written in 1989
Approved by World Health Assembly 1990
Adopted by US 2012

ICD-10: G40 Epilepsy

- G40.0 Localization-related idiopathic epilepsy and epileptic syndromes with seizures of localized onset
- G40.1 Localization-related symptomatic epilepsy and epileptic syndromes with simple partial seizures
- G40.2 Localization-related symptomatic epilepsy and epileptic syndromes with complex partial seizures
- G40.3 Generalized idiopathic epilepsy and epileptic syndromes
- G40.4 Other generalized epilepsy and epileptic syndromes
- G40.5 Special epileptic syndromes
- G40.6 Grand mal seizures, unspecified (with or without petit mal)
- G40.7 Petit mal, unspecified, without grand mal seizures
- G40.8 Other epilepsy
- G40.9 Epilepsy, unspecified

ICD-10: G41 Status epilepticus

- G41.0 Grand mal status epilepticus
- G41.1 Petit mal status epilepticus
- G41.2 Complex partial status epilepticus
- G41.8 Other status epilepticus
- G41.9 Status epilepticus, unspecified

ICD-10: modifiers

G40.00 Localization-related idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable
G40.000 Localization-related idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable, without status epilepticus
G40.01 Localization-related idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable
G40.001 Localization-related idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, with status epilepticus

ICD-10: ‘convulsions’

R50-R69 General symptoms & signs
R56 Convulsions, not elsewhere classified
R56.0 Febrile convulsions
R56.8 Other & unspecified convulsions
Coding in practice: ICD-10

- G40.0 Localization-related idiopathic epilepsy and epileptic syndromes with seizures of localized onset
  - Childhood epilepsy with centrotemporal spikes
- G40.1 Localization-related symptomatic epilepsy and epileptic syndromes with simple partial seizures
  - Attacks without alteration of consciousness
  - Simple partial seizures developing into secondary generalized seizures
- G40.2 Localization-related symptomatic epilepsy and epileptic syndromes with complex partial seizures
  - Attacks with alteration of consciousness
  - Complex partial seizures developing into secondary generalized seizures

Coding in practice: ICD-10

- G40.3 Generalized idiopathic epilepsy & epileptic syndromes
  - Benign myoclonic epilepsy in infancy
  - Benign neonatal convulsions [familial]
  - Childhood absence epilepsy
  - Epilepsy with grand mal seizures on awakening
  - Juvenile myoclonic epilepsy

Coding in practice: ICD-10

- G40.4 Other generalized epilepsy & epileptic syndromes
  - Epilepsy with myoclonic absences
  - Myoclonic-astatic seizures
  - Infantile spasms
  - Lennox-Gastaut syndrome
  - Symptomatic early myoclonic encephalopathy
  - West syndrome

Coding in practice: ICD-10

- G40.5 Special epileptic syndromes
  - Epilepsia partialis continua
  - Epileptic seizures related to alcohol, drugs, hormonal changes, sleep deprivation, stress

Impact on Clinical Care and Practice

- ‘Not intractable’ vs ‘intractable’ reflects severity of illness
- Distinction between ‘epilepsy’ and ‘seizures’