Idiopathic Epilepsy Syndromes

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Seizure Type VS Epileptic Syndrome

- A seizure type is determined by the patient’s behavior and EEG pattern during ictal event
- An epileptic syndrome is defined by:
  - Age
  - Seizure type(s)
  - Etiology
  - Neurological status
  - Natural history
  - EEG (ictal & interictal)
  - Response to AEDs

Classification of Seizure

Classification of Electroclinical Syndromes

Advantage of Determination of Electro-clinical Syndrome

- Drives the etiologic evaluation
- Determines the best choice AEDs
- Suggests duration of AED therapy
- Broad forecasts the prognosis & comorbid
- Useful tool for genetic linkage analysis
Idiopathic Epilepsy Syndromes (IES)

• Idiopathic Generalized Epilepsies (IGE)
  – Childhood absence epilepsy (CAE)
  – Generalized epilepsy with febrile seizures plus (GEFS+)
  – Juvenile myoclonic epilepsy (JME)
  – Epilepsy with myoclonic absences
  – Juvenile absence epilepsy (JAE)
  – Epilepsy with grand mal (generalized tonic-clonic) seizures on awakening
    – Benign myoclonic epilepsy in infancy

• Idiopathic Focal Epilepsies (IFE)
  – Benign childhood epilepsy with centrotemporal spikes (BCECTS)
  – Benign childhood occipital epilepsy (BCOE)
  – Benign familial neonatal/infantile seizures (BFNS, BFNIS, BFIS)
  – Autosomal nocturnal frontal lobe epilepsy (ADNFLE)

A girl with frequent staring spells

Typical Absence Seizures

A sudden onset, interruption of ongoing activities, a blank stare, possibly a brief upward rotation of the eyes.

If the patient is speaking, speech is slowed or interrupted, if walking, he stands transfixed; if eating, the food will stop on his way to the mouth. Usually the patient will be unresponsive when spoken to.

The attack lasts from a few seconds to half a minute and evaporates as rapidly as it commenced.

New ILAE Diagnostic Scheme vs ILAE Classification 1989

(1). The syndromes of JAE, JME and IGE with GTCS only are considered as phenotypical variants of IGE of adolescence

(2). A new syndrome of ‘IGE with GTCS only’ has been proposed to replace ‘epilepsy with GTCS on awakening’

(3). ‘Epilepsy with myoclonic-astatic seizures’ and ‘epilepsy with myoclonic absences’ are included among idiopathi généralised epilepsies; these were previously categorised as symptomatic or cryptogenic generalized epilepsies.

(4). ‘Generalised epilepsy with febrile seizures plus’ is proposed as a new syndrome in development

Typical Absence Seizures

• Absence with impairment of consciousness only.
• Absence with mild clonic components.
• Absence with atonic components.
• Absence with tonic components.
• Absence with automatisms.
• Absence with autonomic components.
• Mixed forms of absence
Absence Epilepsy

<table>
<thead>
<tr>
<th></th>
<th>Absence</th>
<th>CPS</th>
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<tbody>
<tr>
<td>Duration for less than 30 sec</td>
<td>as a rule</td>
<td>exceptional</td>
</tr>
<tr>
<td>Duration for more than 60 sec</td>
<td>exceptional</td>
<td>as a rule</td>
</tr>
<tr>
<td>Daily frequency</td>
<td>as a rule</td>
<td>rare</td>
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<tr>
<td>Simple automatisms</td>
<td>frequent</td>
<td>Frequent</td>
</tr>
<tr>
<td>Complex automatisms</td>
<td>exceptional</td>
<td>Frequent</td>
</tr>
<tr>
<td>Bilateral facial myoclonic jerk</td>
<td>frequent</td>
<td>exceptional</td>
</tr>
<tr>
<td>Sudden onset and termination</td>
<td>as a rule</td>
<td>Frequent</td>
</tr>
<tr>
<td>Postictal symptoms</td>
<td>never</td>
<td>frequent</td>
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</table>

Absence Epilepsy

• Childhood absence epilepsy
• Juvenile absence epilepsy

Childhood Absence Epilepsy

- Incidence: 7/100,000 of children < 15 years
- Onset: mostly 4 - 10 years
- Normal neurological state and development
- Genetics: Polygenic transmission/ some AD
- Induction: Hyperventilation-induced
- Brief (4–20 seconds, exceptionally longer) and frequent (tens per day) absence seizures with abrupt and severe impairment (loss) of consciousness.
- Automatisms are frequent but have no significance in the diagnosis.

EEG
- ictal discharges: generalized high-amplitude 3- Hz-spike and slow wave complexes.
- Spike-wave is rhythmic at around 3 Hz with a gradual and regular slowdown from the initial to the terminal phase of the discharge.
- The duration of the discharges varies from 4 to 20 seconds.
Absence epilepsy: generalized 3 Hz spike-waves induced by hyperventilation

Absence seizure during hyperventilation in a 7 y/o girl

A 15 y/o girl with GTC upon awakening
(after late party and alcohol consumption)
(clumsiness)

Juvenile Absence Epilepsy

- Onset: late childhood, 9 - 13 years
- Seizure:
  - absence seizures
  - Nearly all patients may have GTCS.
  - More than half have myoclonic jerks but these are mild and do not show the circadian distribution of JME.
  - Consistent visual, photosensitive and other sensory precipitation of clinical absences is probably against the diagnosis of JAE.
  - However, on EEG, intermittent photic stimulation often facilitates generalized discharges and absences.

<table>
<thead>
<tr>
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<th>1st GTC</th>
<th>2nd GTC</th>
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<tbody>
<tr>
<td>GTCs with other clinically evident sz</td>
<td>90%</td>
<td>90%</td>
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<tr>
<td>Typical absence</td>
<td>60%</td>
<td>None</td>
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<tr>
<td>Myoclonic</td>
<td>40%</td>
<td>none</td>
</tr>
<tr>
<td>Focal seizure</td>
<td>none</td>
<td>90%</td>
</tr>
<tr>
<td>GTCS without other clinically evident sz</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Precipitating factors</td>
<td>&gt; 60%</td>
<td>&lt; 10%</td>
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<tr>
<td>Consistently on awakening</td>
<td>common</td>
<td>uncommon</td>
</tr>
<tr>
<td>Family history of similar epilepsy</td>
<td>common</td>
<td>uncommon</td>
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<tr>
<td>EEG in untreated patients</td>
<td></td>
<td></td>
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<tr>
<td>Generalized discharges</td>
<td>80</td>
<td>Exceptional</td>
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<tr>
<td>Focal abnormalities alone</td>
<td>10</td>
<td>60</td>
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<tr>
<td>Generalized + focal abnormalities</td>
<td>10</td>
<td>30</td>
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</table>

Treatment & Outcome

- Drugs of choice
  - ethosuximide, valproate, lamotrigine
  - clonazepam, nitrazepam, acetazolamide
- Usually respond to treatment
- Transform to other type of seizure
- Recurrent: not common
- Prognosis: favorable
**Juvenile Myoclonic Epilepsy (Janz Syndrome)**

- Sudden, mild to moderate myoclonic jerks (shoulder & arm) during awake, GTC
- Precipitating: sleep deprivation, alcohol intake, fatigue
- Chromosome 6, AD
- Onset 12 - 18 years (mean 14.6 years)
- Normal examination

**Comparison Between Absence & JME**

<table>
<thead>
<tr>
<th></th>
<th>Childhood</th>
<th>Juvenile</th>
<th>JME</th>
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<tbody>
<tr>
<td>Age of onset</td>
<td>2-12 yrs</td>
<td>puberty</td>
<td>puberty</td>
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<tr>
<td>Frequency</td>
<td>multiple/D</td>
<td>rarely/D</td>
<td>variable</td>
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<tr>
<td>EEG</td>
<td>3 Hz.S+W</td>
<td>3.5-4 Hz S+W</td>
<td>3.5-6 Hz.S+W</td>
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<tr>
<td>GTC</td>
<td>40-60%</td>
<td>80%</td>
<td>80 - 85 %</td>
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<td>ETH, VPA</td>
<td>VPA</td>
<td>VPA</td>
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<tr>
<td>Prognosis</td>
<td>favorable</td>
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</table>

**Age onset of different seizure type in JME**

Age at onset of absences, myoclonic jerks and GTCs in 56 consecutive patients with JME.

[Modified from Panayiotopoulos et al, Epilepsia, 1991]
### Clinical Course & Treatment

- Life-long treatment & respond to AED
  - Valproate (usually low dose)
  - Lamotrigine
  - Benzodiazepines
- Awareness of teratogenic effect of VPA in pregnancy
- Excellent prognosis

### Diagnostic Tips for JME

- GTCS, usually preceded by myoclonic jerks, are nearly pathognomonic of JME if they occur in the morning after:
  - A party to celebrate a birthday, end of school term or New Year’s eve
  - Waking up early in the morning to travel on a vacation, particularly after a late night
  - Replacement of valproate with carbamazepine in women wishing to start a family
  - Withdrawal of appropriate medication after many seizure-free years.

### Idiopathic Generalized Epilepsy with GTC Seizures Only

- Age at onset: 6 to 47 yrs (peak at 16–17 yrs)
- Men (55%) predominate slightly
- GTCS occur exclusively shortly after awakening regardless of the time of day or in a second seizure peak in the evening period of relaxation.
- With age, GTCS tend to increase in frequency and become more unpredictable
- Precipitating: sleep deprivation, alcohol, fatigue, shift work

#### Characteristics

- Genetic predisposition is relatively frequent.
- EEG: generalized epileptiform discharge, photosensitive
- Normal MRI brain
- Lifelong disease
- Treatment: VPA, LTG, LEV

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![Image](image.png)

**Man aged 18 years with 2 GTCs at age 14 and 18 on awakening after sleep deprivation**

There were no clinical manifestations during hyperventilation with breath counting.
### GEFS+

- **Generalized Epilepsy with Febrile Seizures plus**
- **Autosomal Dominant Epilepsy with Febrile Seizures plus**
- GEFS+ has been described by Berkovic and his associates and has been recognized as a syndrome in development by the ILAE Task Force.

#### GEFS+

- **Age at onset:** first months of life to childhood
- **Male = Female**
- **Heterogeneous clinical phenotypes**
  - febrile seizures plus (FS+)
  - non-febrile generalized convulsions, absences, myoclonic, atonic, myoclonic-atonic seizures.
  - focal frontal and temporal lobe seizures may occur

#### Idiopathic Localization-related Epilepsy

- **Benign childhood epilepsy with centrottemporal spikes (BCECTS)**
- **Benign childhood occipital epilepsy (BCOE)**

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**A boy with recurrent febrile seizures from aged of one year to 8 year**

- marked genetic and phenotypic heterogeneity,
- extreme intra-familial and inter-familial clinical variations regarding seizure type, seizure frequency, severity and prognosis.
- SCN1A, SCN1B and SCN2A genes; GABRG2 gene
- Same spectrum with more severe syndromic phenotypes: Dravet syndrome, epilepsy with myoclonic-astatic seizures of Doose

**GEFS+**

- Brain MRI: normal
- EEG: depend on the clinical phenotype,
  - usually normal
  - generalized discharges, focal sharp waves
- Prognosis: usually benign and self-limited
  - non-febrile seizures occur in only 25%, infrequent, often remit by mid-childhood (median 11 years).
- Treatment: valproate, levetiracetam, topiramate
Benign Epilepsy with Centrotemporal Spikes (BECTS)

or

Benign Rolandic Epilepsy

or

Benign Childhood Epilepsy with Centrotemporal Spikes (BCECTs)

Characteristics

1. Onset between 2 and 14 years (3 – 10 years)
2. Simple focal motor seizure
3. Characteristic EEG foci over rolandic (centrotemporal region) with normal posterior dominant rhythm

Clinical Presentations

- Unilateral facial sensorimotor symptoms (>30%)
  - Tingling face or hand
  - Tonic-clonic movements of face or hand
- Oropharyngeal manifestation (>50%)
- Speech arrest (40%)
- Excessive salivation (30%)
- Nocturnal
- Status epilepticus
- Presentation as 1st unprovoked seizure

Benign Epilepsy with Centrotemporal Spikes

- Most common partial epilepsy
  - 10 – 20% of childhood epilepsy
  - 15.7 % of epilepsy before 15 years old
  - 24 % of epilepsy with onset 5 - 14 years
- Male predominance
- Frequent seizures: those with age of onset prior to 3 years

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Benign Epilepsy with Centrotemporal Spikes

- Unclear genetic basis
  - Genetic predisposition (40%)
  - Complex inheritance
  - AD trait, Chromosome 15q14, 16p
  - Mutation of potassium channel gene KCNQ2

Prognosis

- Excellent prognosis
- Spontaneous remission
- Some with neuropsychological disorders
- Evolution to or relationship with
  - Landau-Kleffner syndrome
  - Epilepsy with continuous spike-wave during slow-wave sleep
Investigation

- EEG: Wakeful, drowsy & sleep recording
- Brain imaging
  - Not necessary in typical presentation & EEG findings
  - Non-specific finding may be found in 15% without any affect to decision-making for long-term treatment
- Other blood tests
  - Not necessary

Treatment

- To treat or not to treat: not to be treated with long-term prophylactic AED
- Weigh between risk of seizure and risk of treatment
- Rx may be considered in
  - Repeated frequent seizures
  - Status epilepticus
  - Parents’ request
- Single AED therapy with excellent response

Risk from Treatment

- Adverse effects from antiepileptic drugs
  - Hematopoietic system: aplastic anemia
  - Liver, pancreas, cardiac functions
  - Idiosyncratic drug reactions: SJS, TEN
  - Cognitive dysfunction
  - Mood and behavior problems
  - Others: weight gain or loss, tremor, etc....

Prognosis

- Spontaneous remission by age of 16 years
- Seizure recurrence
  - 2 – 4 yrs after onset
  - 10 - 20% few seizures
- Some children with minor neuropsychiatric or neurodevelopment disability
  - Cognitive dysfunction
  - Learning disability
- Some overlap with Landau-Kleffner syndrome & ESES
Cognitive Dysfunctions & Other Co-morbid

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
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<td>Kumar, S.</td>
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<td>Pediatr Neurol 2008;10:1-8</td>
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<td>Adolph, L.</td>
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Practical points

- EEG during awake and asleep in each epileptic syndrome may have different characteristics
  - BECT: maybe only abnormal during sleep
- Both awake and asleep EEG, as well as certain activation methods should be done in individual patients with different syndrome
  - Absence: hyperventilation
  - JME: sleep deprivation, awaken during EEG

Seizure & Cognitive Outcomes in Thai Children with Benign Rolandic Epilepsy

Cross-section study from 2002 - 2009

46 Children with BRE as the first diagnosis at Ramathibodi Hospital
- 23 boys & 23 girls
- Age range 5 – 14.5 yrs.
- Mean FU duration 19.5 mo.
- 31 pts (67.4%): taking AED
- 15 pts (32.6%): no AED without seizure recurrence

46 Thai children with BRE: IQ & WRAT

Children with BRE

<table>
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<tr>
<th>Test</th>
<th>n</th>
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<tr>
<td>IQ test*</td>
<td>37</td>
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<tr>
<td>WRAT**</td>
<td>30</td>
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Children with BRE

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<tr>
<th></th>
<th>Normal</th>
<th>Abnormal</th>
<th>LD</th>
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<tbody>
<tr>
<td>IQ</td>
<td>31 (83.8%)</td>
<td>6 (16.2%)</td>
<td></td>
</tr>
<tr>
<td>WRAT</td>
<td>10 (33.3%)</td>
<td>20 (66.7%)</td>
<td></td>
</tr>
</tbody>
</table>

*WISC-III (n=36) or Stanford-Binet IV (n=1)
**WRAT: Wide Range Achievement Test - Thai version

Practical point

- Physicians who order the EEG should give adequate information regarding the clinical information and other information to increase yield of diagnosis
  - Absence: adequate hyperventilation
  - BRE: include sleep portion
  - BEOP: include eye open, eye closing
  - JME: include EEG after awakening

THANK YOU FOR YOUR ATTENTION