Recent Management of Childhood Epilepsies

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Definition of Epilepsy

Epilepsy is a recurrent paroxysmal & transitory disturbance of the brain function, which develops suddenly & ceases spontaneously, with or without impairment of consciousness & abnormal electrical activity of the brain.
Etiology

1. Local or focal causes
2. General or systemic causes
3. Constitutional or idiopathic epilepsy
Classification of Epilepsy

- Partial seizures
- Generalized seizures
- Unclassified epileptic seizures
- Status epilepticus
NORMAL EEG IN CHILDREN

- **Awake:** Precentral: beta activity
  Postcentral: Slower alpha &/or theta activity
- **Asleep:** Slow alpha + theta + delta activity
  + sleep spindles + K complexes
Summary of Clinical & EEG Features of Seizures

<table>
<thead>
<tr>
<th>Seizure</th>
<th>Duration</th>
<th>Conscious</th>
<th>Confusion</th>
<th>Ictal EEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple Partial</td>
<td>5-10 sec</td>
<td>Preserv.</td>
<td>no</td>
<td>Normal or focal spikes</td>
</tr>
<tr>
<td>Complex Partial</td>
<td>1-2 min</td>
<td>lost</td>
<td>yes</td>
<td>Focal activity spreading</td>
</tr>
<tr>
<td>Absence</td>
<td>5-10 sec</td>
<td>lost</td>
<td>no</td>
<td>Generalized 3/sec sp&amp;w</td>
</tr>
<tr>
<td>Generalized Tonic Clonic</td>
<td>1-2 min</td>
<td>lost</td>
<td>yes</td>
<td>Generalized spikes</td>
</tr>
</tbody>
</table>
International Classification of Epilepsies & Epileptic Syndromes

1. Localization-Related (Focal, Local, Partial) Epilepsies & Syndromes.
   1.1 Idiopathic with age-related onset
   1.2 Symptomatic

2. Generalized Epilepsies & Syndromes
   2.1 Idiopathic with age-related onset, listed in order of age.
   2.2 Idiopathic &/or symptomatic, in order of age appearance
   2.3 Symptomatic

3. Epilepsies & Syndromes Undetermined as to Whether They Are Focal Or Generalized
   3.1 With both generalized & focal seizures
   3.2 Without unequivocal generalized or focal features

4. Special Syndromes
   4.1 Situation-related seizures
   4.2 Isolated, apparently unprovoked epileptic events
   4.3 Epilepsies characterized by specific modes of seizure precipitation
   4.4 Chronic progressive epilepsia partialis continua of childhood
Infantile Spasms

- Sudden shock-like flexion of the arms, head, neck & trunk, & drawing up of the knees.
- Progressive mental deterioration
- Affect infants & children, boys > girls.
- EEG shows almost continuous irregular slow spike- &-wave activity, called “hypsarrhythmia”
- Syndrome observed in children with hypoglycemia, phenylketonuria, perinatal brain damage & tuberous sclerosis
- Anticonvulsants are relatively ineffective, apart from clonazepam which is effective in some cases
- ACTH is effective in most cases
Pseudoseizures (Psychogenic Seizures)

- Sometimes stimulate "akineti
  c seizures"
- Other seizures can sometimes be
  imitated
- Treated by psychotropic drugs, behavio
  ral therapy, relaxation & biofeedback techniques
**Pediatric Epilepsy Syndromes by Age of Onset**

**NEWBORNS:**
- Benign neonatal convulsions (5th day fits)
- Familial benign neonatal convulsions
- Early myoclonic encephalopathy
- Severe idiopathic status epilepticus

**INFANTS:**
- Febrile convulsions
- West’s syndrome: Infantile spasms
- Benign myoclonic epilepsy in infants
- Severe myoclonic epilepsy in infants
- Epileptic seizures caused by inborn errors of metabolism
- Myoclonic-astatic epilepsy of early childhood
- Lennox-Gastaut syndrome.

**CHILDREN:**
- Childhood absence epilepsy (pyknolepsy)
- Epilepsy with myoclonic absences
- Epilepsy with generalized convulsive seizures
- Benign partial epilepsies
- Benign epilepsy with centrotemporal (rolandic) spikes (BERS)
- Benign psychomotor epilepsy
- Benign epilepsy with occipital spike-waves (BEOSW)
- Other benign partial epilepsies
- Benign partial epilepsy with extreme somatosensory-evoked potentials
- Landau-Kleffner syndrome
- Epilepsy with continuous spikes & waves during sleep
Factors in Febrile Seizures Associated With Increased Risk of Epilepsy at age 7 Years

- Family history of alter epilepsy
- Pre-existing neurologic abnormality
- Complex febrile seizure
  - >15 minutes duration
  - >1 febrile seizure per 24 Hour
- Focal febrile seizure
Paroxysmal Conditions Resembling Epilepsy

A. Narcolepsy
B. Migraine
C. Paroxysmal abdominal pain
D. Breath-holding Spells
E. Hypercyanotic attacks
F. Shuddering Attacks
G. Cardiovascular Syncope
H. Conversion Reaction
I. Malingering
J. Trigeminal Neuralgia
K. Paroxysmal Vertigo
# Anti-Epileptic Drugs (AEDs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Use</th>
<th>Form</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Generalized &amp; Partial</td>
<td>Tab susp</td>
<td>Double vision</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Partial &amp; Myoclonic</td>
<td>Tab amp</td>
<td>drowsiness</td>
</tr>
<tr>
<td>Ethosuximide</td>
<td>Absences only</td>
<td>Caps Syp</td>
<td>nausea</td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>Generalized &amp; Partial</td>
<td>Tab</td>
<td>sedation</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Generalized &amp; Partial</td>
<td>Caps Susp</td>
<td>drowsiness</td>
</tr>
<tr>
<td>Primidone</td>
<td>Generalized &amp; Partial</td>
<td>Tab susp</td>
<td>sedation</td>
</tr>
<tr>
<td>Valproate</td>
<td>Generalized &amp; Partial &amp; Absences</td>
<td>Tab liquid</td>
<td>drowsiness</td>
</tr>
</tbody>
</table>
# New Antiepileptic Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indications</th>
<th>Half-Life</th>
<th>Plasma Binding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clobazam</td>
<td>Partial &amp; generalized</td>
<td>30-46</td>
<td>85%</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Partial &amp; tonic-clonic</td>
<td>8-24</td>
<td>40%</td>
</tr>
<tr>
<td>Tiagabine</td>
<td>Partial &amp; secondary generalized</td>
<td>6-8</td>
<td>96%</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Partial &amp; secondary generalized</td>
<td>20-24</td>
<td>10-20%</td>
</tr>
<tr>
<td>Vigabatrin</td>
<td>Partial &amp; secondary generalized</td>
<td>4-8</td>
<td>Minim</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Partial &amp; secondary generalized</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Partial &amp; secondary generalized</td>
<td>25</td>
<td>54%</td>
</tr>
<tr>
<td>Felbamate</td>
<td>Lennox-Gastaut Syndrome</td>
<td>20-23</td>
<td>22-25%</td>
</tr>
</tbody>
</table>

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# Side Effects of New AEDs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Principal Side Effects</th>
<th>Serious but Rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin</td>
<td>somnolence</td>
<td></td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Rash, dizziness</td>
<td>Stevens-Johnson</td>
</tr>
<tr>
<td>Felbamate</td>
<td>Irritability</td>
<td>Aplastic anemia</td>
</tr>
<tr>
<td>Clobazam</td>
<td>Sedation</td>
<td></td>
</tr>
<tr>
<td>Vigabatrin</td>
<td>Behavioral changes</td>
<td>Psychosis</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Dizziness</td>
<td></td>
</tr>
<tr>
<td>Tiagabine</td>
<td>Confusion</td>
<td></td>
</tr>
<tr>
<td>Topiramate</td>
<td>Cognitive disturbance</td>
<td></td>
</tr>
</tbody>
</table>
## Adverse Effects of New AEDs

<table>
<thead>
<tr>
<th>Ad- Ef</th>
<th>Vigabatrine</th>
<th>Lamotrigine</th>
<th>Carbapentine</th>
<th>Felbamate</th>
<th>Oxcarbazepine</th>
<th>Topiramate</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI upset</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Dizziness</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ataxia</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Somnolence</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>-</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Headache</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Diplopia</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>+</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Fatigue</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Seizure types controlled by new AED’s

- **Partial seizures (without secondary generalization)** ⇒ Lamotrigine
- **Primary Generalized Tonic-Clonic Seizures** ⇒ Topiramate
- **Atonic Seizures** ⇒ Vigabatrin
- **Myoclonic Seizures** ⇒ Clonazepam
- **Absence Seizures** ⇒ Clobazam
Method By Which Compliance Can Be Measured

**DIRECT**
- Measurement of isolated AED levels
- Serial measurement of AED levels determine variability
- Recording pill-taking behavior with electronic device

**INDIRECT**
- Patient interview
- Therapeutic outcome
- Physician’s judgment
- Interviews with caregivers
- Pill counts
Strategies to Improve Patient Compliance

1. Education: Explain plan, discuss timetable, provide pamphlets

2. Dosing: ↓ medications, ↓ doses, provide a bill box

3. Clinic Visits: ↑ frequency of visits, designate specific clinic staff person
## Sports & Epilepsy (Permitted Sports)

<table>
<thead>
<tr>
<th>Aerobics</th>
<th>Curling</th>
<th>Jogging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Archery</td>
<td>Dancing</td>
<td>Lacrosse</td>
</tr>
<tr>
<td>Badminton</td>
<td>Dogs leading</td>
<td>Oreintering</td>
</tr>
<tr>
<td>Ballet</td>
<td>Discus throwing</td>
<td>Short-putting</td>
</tr>
<tr>
<td>Baseball</td>
<td>Fencing</td>
<td>Soccer</td>
</tr>
<tr>
<td>Basketball</td>
<td>Field hockey</td>
<td>Table Tennis</td>
</tr>
<tr>
<td>Bowling</td>
<td>High jumping</td>
<td>Volleyball</td>
</tr>
<tr>
<td>Broad Jumping</td>
<td>Fishing</td>
<td>Weight lifting</td>
</tr>
<tr>
<td>Cricket</td>
<td>Gymnastics</td>
<td>Wrestling</td>
</tr>
</tbody>
</table>
Sports & Epilepsy (Possible Sports)

- Bicycling
- Diving
- Football
- Hockey
- Hunting Mountain climbing
- Sailing
- Swimming
Sports & Epilepsy (Prohibited Sports)

- Boxing
- Polo
- Rock climbing
- Surfing
- Scuba diving
- Snorkeling
- Waterskiing
FEBRILE CONVULSIONS

- Convulsions accompanying febrile illness & early childhood (between 3 months & 5 years of age) without evidence of I.C. infection or defined cause
- Two-thirds of young children experiencing convulsions have febrile seizures only
- Febrile convulsions are generalized tonic clonic
- They tend to cluster in families (10-20% of siblings)
- <5% develop non-febrile seizures
Management of Febrile Convulsions

- **Control fever** by sponging & antipyretics
- **Control convulsions** by I.V. diazepam 0.3mg/kg
- **Intermittent rectal diazepam therapy** at the onset of fever or at the onset of a seizure
- **Chronic treatment** by Phenobarbital (4-5mg/kg) in a single nocturnal dose for 2 yrs OR:
- **Chronic treatment** by Sod. Valproate (20-30 mg/kg/d) for 1 yr
Intractable Epilepsy

- 70-80% of newly diagnosed epileptics satisfactorily respond to AEDs
- 20-30% of patients develop chronic or intractable epilepsy despite AED therapy
- Seizure frequency, type, circadian occurrence, number of AEDs that have been tried, impact of seizures on daily life, all determine intractability
- Intractable epilepsy may be controlled by surgery, vagus nerve stimulation, ketogenic diet, or behavior modification strategies
Intractability

“Persistence of true epileptic seizures with a sufficient frequency &/or severity in a compliant patient despite optimal therapy during a minimum of two years.”
Indicators of Poor Prognosis of Epilepsy

- **Organic brain lesion**
- **Partial seizures**
- **Multiple seizure types**
- **High number of seizures**
- **Seizure onset in infancy**
- **Abnormal background EEG activity**
- **Generalized paroxysms in the EEG**
Therapeutic Options in Intractable Epilepsy

1. **Surgery:** e.g. “temporal lobectomy” \(\Rightarrow\) 70-80% seizure freedom in “mesial temporal sclerosis”

2. **Vagus nerve stimulation:** is usually in intractable partial seizures

3. **Conditioning and behaviour modification techniques**

4. Progressive **relaxation** training

5. **A reduction** of no. of AEDs used
Pseudo-epileptic Seizures in Children (Non-epileptic Seizures)

- Occasional situational epileptic seizures
- Involuntary movement disorders
- Parasomnias
- Diurnal psychic episodes
- Migraine attacks
- Gastro-intestinal disturbances
- Brain stem compression
Intractable Seizures & Epilepsies in Infancy & Early Childhood

There is a triad of intractable epileptic syndromes in infancy & early childhood:

1. Early infantile encephalopathy (Ohtahara Syndrome)
2. West syndrome (Infantile Spasms)
3. Lennox-Gastaut Syndrome
Characteristics of Early Infantile Epileptic Encephalopathy

- **Seizures:**
  1. Onset in early infancy
  2. Multiple etiology
  3. Intractable

- Suppression-first burst in EEG, awake & sleep
- Severe psychomotor retardation
- Evolution into the West Syndrome
Characteristics of West Syndromes

- It has 3 typical features:
  1. Infantile spasm
  2. Hyspsarrhythmia in the EEG &
  3. Mental retardation in 90%

- PET classified (Infantile Spasms) by etiology into:
  1. Symptomatic type
  2. Cryptogenic type
  3. Idiopathic type

- Symptomatic & Cryptomatic infantile spasms are intractable
- Idiopathic type has a good prognosis
- The seizures of West syndrome are intractable in 55-85%
Characteristics of the Lennox-Gastaut Syndrome

- **Epileptic seizures**
  - Atypical absences
  - Axial tonic seizures
- **Waking EEG**
  - Diffused slow interictal spikes & waves
- **Sleep EEG**
  - Fast (10HZ) rhythmic bursts
- **Slow mental development**
- **Personality disturbances**
Intractable Seizures & Epilepsies in Adolescence

- Many partial seizures, particularly CPSs are intractable
- Leisonal partial epilepsies may cause scholastic, cognitive, & psychosocial problems
- GTCSs associated with juvenile absence epilepsy may be drug-resistant
Factors of Poor Prognosis & Intractability of Childhood Epilepsy

- Onset of epilepsy in infancy
- Symptomatic etiology of seizures
- Presence of a neurologic deficit
- Neurotic or psychotic disturbances
- Abnormal EEG
- Presence of multiple seizure types
- Poor response to therapy
Psychosocial Consequences of Intractable Epilepsy in Children

What happens to the child after the onset of epilepsy?

1. Dread, anxiety, guilty shame, sorrow, anger
2. Hospitalization, visits to physicians
3. Medication, side effects
4. Interruptions in daily life
5. Changes in habits
Siblings of the Child With Epilepsy Exhibit Specific Reactions:

• **Physical complaints**
  *Headache, gastric pain & symptoms similar to those of the patients*

• **Psychic complaints**
  *Fear of being alone, afraid of the dark, fear of becoming sick or of dying, nightmares & sleep disturbances, dread of hospitals & physicians, & fear of losing the parents love*
Crisis in the Family & Lack of Adaptation to the Child’s Condition May be a Result of:

- Changes in frequency of seizures
- Changes in types of seizures
- Changes in medications
- New side effects
- Emergence of new, or newly recognized physical or psychic handicaps
- Further development of existing difficulties, e.g. poor scholastic achievement
New Drugs for Intractable Epilepsy (New AEDs)

- Clobazam
- Felbamate
- Gabapentin
- Lamotrigine
- Oxcarbazepine
- Vigabatrine
- Tiagabine
- Topiramate
Indications for Epilepsy Surgery

- Epilepsy surgery is considered to be the last result & is reserved for intolerable & intractable epilepsies
- Adverse effects include increased morbidity & mortality
- However, the outcome is good both with regards to seizures & quality of life
- We should operate before the functional or psychosocial consequences have become devastating or irreversible
Contraindications for Epilepsy Surgery

- **Grave mental retardation**
- **Psychosis**
- **Old age** may decrease the chances of improved Q.O.L. & increased the chances of post operative morbidity
- **Grave behavioral disturbances & personality disorders**
- **Post operative sequelae** should not be greater than the preoperative problems
Vagal Nerve Stimulation for Treatment of Intractable Epilepsy

- **Convention AEDs** ⇒ seizure controlled in 70%
- **New AEDs** ⇒ seizure controlled in additional 5-10%
- **Epilepsy surgery** is an effective therapy for some patients
- **Vagal nerve stimulation (VNS)** ⇒ anti-convulsant effects in patients with refractory partial seizures
- **VNS** is achieved through chronic intermittent stimulation of the left vagal nerve
Neurocybernetic Prosthesis (NCV) System

- An implantable pulse generator & stimulating lead with unique helical electrodes, that together deliver programmable pulse trains to the left vagus nerves 24 hrs a day.
- A hand-held magnet may be used to activate the generator transcutaneously if the patient experiences an aura.
- The generator may be programmed externally.
- The battery is expected to loss 36-60 months.
- After battery depletion, the pulse generator must be replaced.
Is Intractable Epilepsy Preventable?

- **Two approaches to limit intractable epilepsy:** Primary prevention & administration of AEDs
- **The more seizures that have occurred before treatment,** the worst the prognosis
- **The longer the seizures continue after AEDs are commended,** the worse the long-term prognosis
- **Benign Rolandic epilepsy** (Focal motor seizures in face, throat & arm, nocturnal, between 7-12 yrs, seizures stop spontaneously by mid-adolescence)
- **Juvenile myoclonic epilepsy** (In adolescence, ⇒ early morning myoclonus + TCSs + generalized spike & wave in the EEG, responds to valproate)
- **Good compliance** decrease the possibility of failure of AED treatment
- **Many epileptics whom doctors believed that they had cured** had probably had a spontaneous remission
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