Evaluation of the First Seizure and New Onset Epilepsy

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Hauser 1990: US Incidence Estimate

- **Febrile**: Approximately 100,000 per year
- **Epilepsy**: Approximately 20,000 per year
- **Acute S.**: Approximately 10,000 per year
- **Seizures**: Approximately 10,000 per year

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Hauser, 1990

- Epilepsy, 1% of population
- Neonatal seizures (NS), 0.1% of population; 33% will develop epilepsy
- 0.3% prior NS
- 5% to 10% prior AS
- 10% to 15% prior FC
- 15% to 20% will develop epilepsy
- Acute symptomatic (AS) (nonfebrile), 0.5% of population
- Febrile convulsions (FC), 2% to 4% of population
- 3% to 5% will develop epilepsy
Importance of Epilepsy Etiology

- Prognosis
- Treatment
Etiology

- Idiopathic
- Congenital
- Trauma
- Vascular
- Neoplasm

Comparison of etiology in children versus adults.
<table>
<thead>
<tr>
<th>EPILEPSY</th>
<th>GENE</th>
<th>FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>BFNC</td>
<td>KCNQ2 and KCNQ3</td>
<td>Voltage- K channel</td>
</tr>
<tr>
<td>GEFS+</td>
<td>SCN1B, SCN1A, and SCN2A</td>
<td>Voltage- Na channel</td>
</tr>
<tr>
<td>ADNFLE</td>
<td>CHRNA4 or CHRNB</td>
<td>Acetylcholine</td>
</tr>
</tbody>
</table>
First Seizure

- Provoked - may require emergent evaluation
- Unprovoked - usually there is time for reflection
Non-epileptic Events

- Breath holding
- Cardiac syncope
- Movement Disorders
- Stimulatory Behaviors
- Migraine
- Psychogenic
AAN/CNS Consensus Statement

• Laboratory studies
  – only if clinically indicated (consider toxicology)
• LP
  – only if indicated clinically
• Imaging
  – MRI is preferred. Acute imaging only if indicated.
• EEG:
  – INDICATED (Standard)
Evaluation of the first unprovoked seizure

- History
- Targeted physical examination
- EEG
- Sometimes brain imaging
Impact of First Seizure Guidelines

- Study at Children’s Memorial
- 60 patients before guidelines instituted
- 120 patients after guidelines
- Marked reduction in admissions and drug administration
- Marked reduction in testing and costs
Evaluation of the First Seizure

• Physical Examination
  – Acute symptomatic causes
    • Focal findings, alteration of mentation, clues from history
  – Underlying predispositions
    • Phakomatoses

• Laboratory - only if indicated
  – CBC, electrolytes, GLUCOSE, Ca++, Mg++, toxic.

• LP, if evidence of CNS infection
EEG is Useful

- Risk of recurrence
- Seizure type
- Epilepsy syndrome predisposition
- Screen for focal abnormalities
Imaging

- MRI
- CT for trauma, other acute provoked seizures
Historical Tips

• History
  – Setting
  – Sequence
  – Show-me
• Development
• Family History
Prognosis after the first unprovoked seizure


- Prospective, 402 children
- Mean follow up was 6.3 YRS.
Shinnar et al

- Recurrence risk: 42%
- Mean time to recurrence: 11.3 MOS.
Shinnar et al

- Risk Factors for Recurrence:
  - Remote symptomatic etiology
  - Abnormal EEG
  - Nocturnal seizure
  - Previous febrile seizure
  - Todd’s paresis
Classic Treatment Works

The First Seizure: Treatment Issues

British Pediatric AED Study

AEDs: comparative efficacy

- Lancet 1996;347:709-13
- M de Silva et al.
- Ages 3-16 years, 2 GTCs or P± GTCs
- 167 children randomised to PB, PHY, CBZ, or VPA
- Starting doses (mg/kg/d)= 3,5,8,15
- Increments of 2,2,4,5
Classic Drugs are Equally Effective

M de Silva et al, 1996 % Seizure Free

0 5 10 15 20 25 30 35 40
12 24 36

PB PHT CBZ VPA
Classic Drugs Have Same Outcome

Time to One Year Remission

- PB
- PHT
- CBZ
- VPA
Data for Adults-VA Cooperative

Cumulative Percentage of Patients with Partial Seizures Successfully Treated with Each Drug During 36 Months of Follow-up

% Continuing

Months

PB denotes phenobarbital, PHT phenytoin, PRM primidone, and CBZ carbamazepine. There were 105 patients at 12 months, 67 at 24 months, and 37 at 36 months.

(NEJM 1985;313:149)
Data for Children

Pellock et al. 1991
New Medications

• **Broad spectrum**
  – Levetiracetam (Keppra)
  – Topiramate (Topamax)
  – Zonisamide (Zonegran)
  – Felbamat (Felbatal)

• **Narrow spectrum**
  – Oxcarbazepine (Trileptal)
  – Gabapentin (Neurontin)
  – Tiagabine (Gabatril)
Matching the AED to the Child

- Co-existent Conditions
- Compliance
- Concurrent Medications
- Cosmetic Concerns
- Prior Drug Reactions
## Summary of AAN evidence-based guidelines level A or B recommendations

<table>
<thead>
<tr>
<th>AED</th>
<th>Newly Diagnosed Monotherapy</th>
<th>Newly Diagnosed Absence</th>
</tr>
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<tbody>
<tr>
<td></td>
<td><strong>Partial/mixed</strong></td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Yes*</td>
<td>No</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Yes*</td>
<td>Yes*</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Yes*</td>
<td>No</td>
</tr>
<tr>
<td>Tiagabine</td>
<td>No</td>
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*Not FDA approved for this indication*
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<tr>
<td>Oxcarbazepine</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Zonisamide</td>
<td>No</td>
<td>No</td>
</tr>
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*Not FDA approved for this indication*
Herrenz et al.
Cognitive side effects of antiepileptic drugs in children

- Authoritative review of literature
Phenobarbital

- Lingering effects on academic achievement 3- 5 years later
Phenobarbital

- Effects on attention
- Reduced processing efficiency
Carbamazepine

- No effect on global IQ
- Modest effect on memory
Phenytoin

- Smaller effect on IQ compared with PB
- Similar effects upon memory c/w CBZ
Valproate

- Small study, valproate had fewer negative effects upon memory than CBZ or PHT.
- Less pronounced effect than PB upon IQ, memory and academic achievement.
New Drugs

- No formal neuropsychological investigations
- All report some drowsiness
- GBP- aggressive behavior Wolf et al, Tallian et al.
- LTG- some improvements
New Drugs

- TGB- asthenia (19%), nervousness (10%) and somnolence (17%) Uldall Et al, 2000.
- TPM- emotional lability 12%, fatigue 15%, difficulty with attention and concentration 12% forgetfulness/impaired memory 7%. Study of 86 children, Elterman et al, 1999.
- VGB- antisocial behavior, irritability and excitability. Zamponi et al.
- ZNS- psychosis, obsessive-compulsive symptoms
Remission Rates, Sillanpaa et al, 1998; 30 year follow-up
Sillanpaa et al, 1998

- Completed only six years of school 2.13
- Unemployed 3.76
- Not married 3.5
- No children 3.0
What does this mean?

- Epilepsy is more than just 2 seizures
School Problems

- A - attention
- B - behavior
- C - cognition
- D - disability, depression, drugs (AEDs)
- E - expectations
What is out there?

- **Newer Treatments**
  - “Neuroprotective”

- **Newer Studies**
  - other outcome measures including development;
  - collaborative designs

- **Comprehensive treatment plans**