Prayer of the Epileptologist

Lord, grant that my work increase knowledge and help other men.
Failing that, Lord, grant that it will not lead to man's destruction.
Failing that, Lord, grant that my article in “Epilepsia” be published before the destruction takes place.

Walker Percy
Epilepsy in Long Term Care Patients
Old Concepts and New Data

Amir Arain, M.D.
Vanderbilt University
Long term care patients

- Patients with mental retardation and developmental disability
- Geriatric patients
Seizures in Patients with MR/DD

• 1/5\textsuperscript{th} of the population of intellectually disabled have epilepsy
• Incidence greatly varies with epidemiological methods.
• In this population, there is a high incidence of confounding nonepileptic events
• Uncontrolled seizures effect the life of individuals and care takers alike regardless of intellectual disability
In several studies epilepsy risk has been positively correlated with severity of MR.

Jacobson et al, 1983: N=44,000
- 95% had MR
- Epilepsy in 23% and CP in 16%
- Epilepsy in 9% of mild MR and 43% of severe MR
- CP in 9% of mild MR and 29% of severe MR
Types of Seizures

• In population based studies GTC most common
  Forsgren et al 1990
• Institution based studies CPS +/- GTC most common
  Mariani et al 1993
• Tonic, atonic, myoclonic and atypical absence seizures are also seen.
• Seizure types are age related
  – GTC and CPS predominate at later ages
Seizure classification

• ILAE classification is not easily applicable to mentally retarded epileptic patients
  – < 34% could classified by Mansford et al 1992
  – < 28% could classified by Mariani et al 1993
Tonic seizures
Atonic seizures
Differential diagnosis

- 2/3\textsuperscript{rd} institutionalized patients with intellectual disability have stereotypical behavior e.g. head movements, rocking and jerking
  Berkson & Davenport 1962

- Medication side effects e.g. tardive dyskinesia can mimic seizure
  Paul 1997
Morbidity

Several factors have an impact on the caring of intellectually disabled individual
– Maladaptive behavior
– Severity of intellectual disability
– Presence of multiple disabilities
– Level of social support
Maladaptive behavior & psychiatric disorder

- Espie et al. found people with double disability showed poor life skills than peers.
- Aggression & self-injurious behavior strongly associated with frequent seizures and antiepileptic polytherapy.
Morbidity of the Care-givers

• 108 children with epilepsy, presence of intellectual disability had a significant impact on caregivers  
  Hoare 1993

• Carers experience stress and prone to clinical anxiety & depression  
Physical morbidity

- Intellectually disabled have high incidence of vitamin D deficiency (Wageman et al 1998)
- Concomitant use of antiepileptic medication can be an additional factor
- Intellectually disabled with epilepsy have a much higher rate of fracture.
Mortality

- Patients with epilepsy have increased risk of mortality
- Patients with intellectual disability have increased risk of mortality
- The risk of mortality is even higher in epilepsy patients with intellectual disability
Seizures provoking factors

- Fever
- Infection
- Constipation
- Noncompliance with medications
- Medications side effects
Treatment: General principles

- Several factors, besides seizures, need special attention.
- Therapy should not focus solely on seizure freedom. These patients already have limited quality of life that needs to be preserved and enhanced.
Cognitive Side effects

- Investigation/treatment hampered by lack of communication
- CNS side effects of antiepileptic drugs may be masked.
- Drowsiness, mood change and behavioral problems may represent toxicity
- Side effects may manifest as behavioral problem

Devinsky 1995
Antiepileptic medications

Drug compliance
Cooperation difficulties, swallowing difficulty
Drugs available as liquid, in soluble form, as powder or as granular may be useful
Rectal suppository and IV formulation
Caregivers are extremely important
In mild MR drug dispensers & alarm watches
Worsening of Seizures

• Some AEDs may have paradoxical effect
• Can be due to overdose or specific effect
• Phenytoin encephalopathy can manifest as frequent seizures 
  \[\text{livanainen 1987}\]
• Carbamazepine can worsen symptomatic
  – atypical absence \[\text{Lerman 1986}\]
  – GTC seizures \[\text{Snead and Hosey, 1985}\]
Worsening of Seizures

• Benzodiazepines can worsen tonic seizures in Lennox-Gastaut syndrome.  
  *Homan et al 1997*

• Vigabatrin can worsen absence, myoclonic, tonic and GTC seizures

• Lamictal may worsen severe myoclonic epilepsy of infancy
  *Guerrini et al 1998*

• Many AEDs may cause enhanced aggressiveness & violence in MR patients
  *Beran &Gibson, 1998*
Treatment

• Alvarez (1989) suggested AED withdrawal after 2 yrs.
  – N= 50
  – Recurrence of seizures 26 patients 52%
  – 11 patients had recurrence during withdrawal
  – 80% of discontinuation happened <3yrs.
Predictors of successful discontinuation

• History of few documented seizures
• No gross neurological abnormalities
• Non therapeutic levels at discontinuation
• Persistent normal EEG pre and post discontinuation
Surgical treatment

• An IQ< 70 was considered a relative contraindication for surgical treatment  Engel 1993
• If the seizure onset is focal from a brain lesion resective surgery should be considered irrespective of the IQ.
• In older patients the chances for multiple epileptogenic lesions is high
• Early intervention may prevent worsening
Geriatric Epilepsy
Age-Specific Incidence of Epilepsy by Gender in Rochester, Minnesota: 1935-1984

Incidence of unprovoked seizures and epilepsy in Iceland

Incidence of all unprovoked seizures by age in Iceland from 1995 to 1999

Epilepsy in the Elderly

- Epilepsy cases rise sharply after age 60
- Incidence at age 50 years is ~ 28/100,000/yr
- Incidence at 60 years is 40/100,000/yr
- Incidence at 75 years is 139/100,000/yr
Demographics

• Different for younger people with epilepsy
Elderly (>65 years)

- Incidence of Alzheimer's: 123/100,000
- Incidence of Epilepsy: 134/100,000

Olmsted County Data
Epilepsy in the Elderly: Incidence and Etiology

Factors Associated With an Altered Risk of Epilepsy

- Family history of seizures: 2.5
- Severe military head trauma: 25
- Severe civilian head trauma: 22
- Moderate head trauma: 16.2
- Mild head trauma: 10
- Stroke: 4.2
- Viral encephalitis: 3.6
- Alzheimer's disease: 2.3
- Bacterial meningitis: 10.1
- Multiple sclerosis: 2.6
- Aseptic meningitis: 0.36
- Alcohol: 1
- Heroin: 1
- Marijuana: 1
- No adverse exposure: 1

*Not statistically significant.

Adapted with permission from Hauser WA, Hesdorffer DC. Epilepsy Foundation of America. 1990
Epilepsy in the Elderly:
Seizure Type

- Complex Partial 38%
- Generalized Tonic-Clonic 27%
- Simple Partial 14%
- Mixed 20%

VA Co-op 2003
n=593
### Epilepsy in the Elderly: Concurrent diseases

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>64%</td>
</tr>
<tr>
<td>Stroke</td>
<td>53%</td>
</tr>
<tr>
<td>Cardiac Disease</td>
<td>49%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>27%</td>
</tr>
<tr>
<td>History of Cancer</td>
<td>22%</td>
</tr>
</tbody>
</table>

VA Co-op 2003
n=593
Epilepsy in the Elderly: Imaging

- Normal 18%
- CVA 44%
- Small vessel disease 40%
- Diffuse atrophy 35%
- Encephalomalacia 9%

VA Co-op 2003
n=593
Epilepsy in the Elderly: EEG

- Normal: 31%
- Epileptiform: 39%
- Focal Slow: 40%
- Generalized Slow: 16%

VA Co-op 2003
n=593
Stroke As A Cause Of Epilepsy

- Annual Incidence of Stroke (Williams, 2001)
  - 750,000 in U.S. (1996)
- Seizures after Stroke Cooperative Study (Bladin, 2000)
  - Prospective, 9-month follow-up, n=2021
  - Seizures in 8.9%
  - 2.3% recurrent seizures
Table 1: Risk Factors for Developing Seizures

<table>
<thead>
<tr>
<th></th>
<th>Patients with seizures,</th>
<th>Patients without seizures,</th>
<th>Significance(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of stroke</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>13 (7)</td>
<td>170 (93)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>9 (25)</td>
<td>27 (75)</td>
<td></td>
</tr>
<tr>
<td><strong>Location of lesion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical</td>
<td>16 (17)</td>
<td>77 (83)</td>
<td>0.01</td>
</tr>
<tr>
<td>Subcortical</td>
<td>6 (4.7)</td>
<td>120 (95.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Size of lesion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large</td>
<td>14 (21.2)</td>
<td>52 (78.8)</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>8 (5.2)</td>
<td>145 (94.8)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

\(^a\) Chi-square.
Table 2: Time Between Symptomatic Supratentorial Brain Infarct and First Seizure in 58 of 65 Patients with Post-infarct Epilepsy, Registered in the MECR (in seven times of stroke not certified).

<table>
<thead>
<tr>
<th>Seizure Delay</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 weeks</td>
<td>14</td>
<td>24%</td>
</tr>
<tr>
<td>&gt;2 weeks - ≤1 Year</td>
<td>22</td>
<td>38%</td>
</tr>
<tr>
<td>&gt;1 year - ≤2 years</td>
<td>11</td>
<td>19%</td>
</tr>
<tr>
<td>&gt;2 years</td>
<td>11</td>
<td>19%</td>
</tr>
</tbody>
</table>
Table 3: Infarct Types on CT in 38 Patients With Epileptic Seizures After Symptomatic Supratentorial Brain Infarction

<table>
<thead>
<tr>
<th>Infarct Type</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical infarct(s) only*</td>
<td>28 (73.7)</td>
</tr>
<tr>
<td>Lacunar infarcts(s) only†</td>
<td>6 (15.8)</td>
</tr>
<tr>
<td>Cortical and lacunar infarct</td>
<td>2 (5.3)</td>
</tr>
<tr>
<td>Cortical and striatocapsular infarct</td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Cortical and watershed infarct</td>
<td>1 (2.6)</td>
</tr>
</tbody>
</table>

* Six had two infarcts
† Three had two infarcts, one had seven infarcts
Seizures in Alzheimers

- Autopsy verified, n=81
- 10% had seizures

Hauser, 1986
Epilepsy in the Elderly

- Epilepsy in the elderly is often misdiagnosed
Delay In Diagnosis
VA Co-op Subset (n=167), 2003

• 9 months to seek medical attention
• 1.7 years to correct diagnosis
• GTC: immediate diagnosis in 67%
  – Less dramatic seizures often ignored
• Concomitant cardiac or cerebrovascular disease caused delays in diagnosis

Spitz, et al
Diagnosis of Epilepsy: Elderly Compared to Younger People

- Higher percentage of partial seizures
- More extra-temporal onset complex partial seizures (missing classic auras)
- More prominent post-ictal symptoms
- Weaker historians
- EEG less helpful
- More concomitant illnesses
Some Diagnostic Dilemmas

- GTC vs. syncope
- Complex partial seizure vs. TIA
- Transient Global Amnesia
## GTC Compared to Syncope

<table>
<thead>
<tr>
<th></th>
<th>GTC</th>
<th>Syncope</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of Cardiac Disease</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Positional</td>
<td>Variable</td>
<td>Orthostatic</td>
</tr>
<tr>
<td>Warning</td>
<td>Variable</td>
<td>Pre-syncope</td>
</tr>
<tr>
<td>Tongue biting</td>
<td><strong>Common</strong></td>
<td>Unlikely</td>
</tr>
<tr>
<td>Complexion</td>
<td>Normal</td>
<td><strong>Pale</strong></td>
</tr>
<tr>
<td>After Event</td>
<td><strong>Confused, sleepy</strong></td>
<td>Alert</td>
</tr>
<tr>
<td>Movements</td>
<td>Tonic-clonic</td>
<td>Loss of tone, brief clonic movements</td>
</tr>
<tr>
<td>Duration</td>
<td>1-2 minutes</td>
<td>seconds to minutes</td>
</tr>
<tr>
<td></td>
<td>then post-ictal</td>
<td></td>
</tr>
<tr>
<td>Incontinence</td>
<td>varies</td>
<td>varies</td>
</tr>
</tbody>
</table>
## Complex Partial Seizures Compared to TIA

<table>
<thead>
<tr>
<th>Feature</th>
<th>CPS</th>
<th>TIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hx of CV Disease</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Anatomic distribution</td>
<td>Not Vascular</td>
<td>Vascular</td>
</tr>
<tr>
<td>Confusion, unresponsiveness</td>
<td>Present</td>
<td>Absent (may be aphasic)</td>
</tr>
<tr>
<td>Frequency</td>
<td>Can be frequent</td>
<td>Rarely frequent</td>
</tr>
<tr>
<td>Amnesia</td>
<td>Common</td>
<td>Absent</td>
</tr>
<tr>
<td>“Aura”</td>
<td>Common</td>
<td>Absent</td>
</tr>
<tr>
<td>Automatisms</td>
<td>Common</td>
<td>Absent</td>
</tr>
</tbody>
</table>
Treat or not to Treat

- The risk of recurrence of seizures is about 30-35% after the first unprovoked seizure.
- The risk of recurrence is about 70% after the second seizure.
- Recurrence rate in elderly.
Epilepsy in the Elderly: Pharmacokinetics and Drug Interactions
70% of new onset Epilepsy patients were first seen by non-neurologists
Determinants of Quality of Life in Patients with Epilepsy

Relationship Between Seizure Frequency and Quality of Life

n = 195  
(r = .01, P = .93)

Determinants of Quality of Life in Patients with Epilepsy

Relationship Between Adverse Events and Quality of Life


n = 195  
(partial correlation \( r = .061 \),  
\( P < .001 \))
<table>
<thead>
<tr>
<th></th>
<th>PHT</th>
<th>CBZ</th>
<th>VPA</th>
<th>PHB</th>
<th>PMD</th>
<th>ESX</th>
<th>CZP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bioavailability</strong></td>
<td>&gt;90%</td>
<td>75-85%</td>
<td>&gt;90%</td>
<td>&gt;90%</td>
<td>&gt;90%</td>
<td>&gt;90%</td>
<td>&gt;80%</td>
</tr>
<tr>
<td><strong>Protein binding</strong></td>
<td>90%</td>
<td>75%</td>
<td>90%</td>
<td>45%</td>
<td>&lt;20%</td>
<td>&lt;10%</td>
<td>86%</td>
</tr>
<tr>
<td><strong>% Metabolism</strong></td>
<td>95%</td>
<td>&gt;95%</td>
<td>&gt;96%</td>
<td></td>
<td>&lt;80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Metabolism site</strong></td>
<td>Liver</td>
<td>Liver</td>
<td>Liver</td>
<td>Liver</td>
<td>Liver</td>
<td>Liver</td>
<td>Liver</td>
</tr>
<tr>
<td><strong>T1/2</strong></td>
<td>7-42</td>
<td>6-20</td>
<td>5-15</td>
<td>65-110</td>
<td>8-15</td>
<td>30-60</td>
<td>30-40</td>
</tr>
<tr>
<td><strong>Autoinduction</strong></td>
<td>no</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>
Are AED Pharmacokinetics and Drug Interactions in the Elderly Important Issues?

- Medication use is greatest in old age
- Older AEDs are frequently prescribed to elderly\textsuperscript{1,2}
- AED efficacy and safety profiles differ from younger patients
- Pharmacokinetics change with age
- Greater risk of drug interactions

Co-Medication Use in Elderly Nursing Home Residents on AEDs

Drug Category

- Antidepressants: 19%
- Antipsychotics: 12.7%
- Benzodiazepines: 22%
- Thyroid Supplements: 14%
- Antacids: 8%
- Antiepileptic Drugs: 12%
- Calcium Channel Blockers: 7%
- Warfarin: 5.9%
- Cimetidine: 2.5%

Maintenance Medication Use by Elderly Nursing Home Residents

+ AED: 6 meds
- AED: 5 meds

AED Efficacy and Safety in the Elderly

Elderly
• Appear more responsive to AED therapy at lower concentrations
• Have an increased risk of adverse reactions
Physiological Changes of Aging Affecting AED Pharmacokinetics

- △ in GI anatomy: variable absorption
- ↓ Serum albumin: altered protein binding
- ↓ Hepatic blood flow
- ↓ Liver Mass
- ↓ Oxidative reactions (↓ 1%/yr › 40 yrs)
- ↓ or – conjugation reactions?
- ↓ Induction of microsomal enzymes?
- ↓ Glomerular filtration (↓ 1%/yr › 40 yrs)
- Disease may exacerbate physiologic changes

However, there are few AED pharmacokinetic studies in the elderly, esp. oldest-old (≥ 85)
AED Pharmacokinetics in the Elderly: Protein Binding

- Several AEDs are highly bound to serum proteins, primarily albumin
  - Carbamazepine 75-85%*  
  - Phenytoin 90%  
  - Valproate 80-95%  
  - Tiagabine 96%

  * CBZ binds to both albumin and alpha 1 acid glycoprotein (AAG)

- Changes in protein binding cause misleading measurement of total concentration of highly bound AEDs

Use of AED ER Formulations in the Elderly

- Elderly are at greater risk for noncompliance due to # of medications and cognitive impairment

- Elderly may be more susceptible Cmax-related side effects, particularly from rapidly absorbed AEDs

- ER formulations may
  - Enhance compliance by reducing dosing frequency
  - Improve therapeutic outcomes
  - Decrease peak-related side effects
  - Improved efficacy with higher blood levels
  - Decrease nursing medication administration time
## Isoenzyme-Mediated AED Metabolism and Drug Interactions

<table>
<thead>
<tr>
<th>AED Substrates</th>
<th>CYP 1A2</th>
<th>CYP 2C9</th>
<th>CYP 2C19</th>
<th>CYP 3A4*</th>
<th>UGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBZ (minor)</td>
<td></td>
<td></td>
<td>Diazepam</td>
<td>CBZ epoxidation</td>
<td>Lorazepam</td>
</tr>
<tr>
<td>PB</td>
<td></td>
<td></td>
<td></td>
<td>Clonazepam</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>VPA</td>
<td></td>
<td></td>
<td>PHT (minor)</td>
<td>Diazepam</td>
<td>MHD</td>
</tr>
<tr>
<td>(minor)</td>
<td></td>
<td></td>
<td></td>
<td>Felbamate</td>
<td>VPA</td>
</tr>
</tbody>
</table>

### Inhibitors

- Cimetidine
- Ciprofloxacin
- Enoxacin
- Fluvoxamine
- Tacrine
- Ticlopidine
- Amiodarone
- Cimetidine
- Felbamate
- Fluconazole
- Fluoxetine
- Fluavastatin
- Isoniazid
- Losartan
- Ticlopidine
- Fluvoxamine
- OXC, MHD (weak)
- Omeprazole
- Ticlopidine
- TP

### Inducers

- Cigarette smoke
- Omeprazole
- Charbroiled meats
- CBZ
- Rifampin
- St. John’s wort
- Dexamethasone
- Phenytoin
- Phenobarbital
- Rifampin
- Rifapentine
- St. John’s wort
- CBZ
- PHT
- PB
- Rifampin
- Rifapentine
- Rifabutin
- St. John’s wort

* CYP3A4: catalyzes biotransformation of 50% of all drug undergoing metabolism
Relationship of PHT Half-Life with Age

Cloyd et al, 2004
Phenytoin-Simulated Dosing Requirements in Elderly vs Younger Adults

Differences in PHT Content:
Capsules 92%
Infatabs 100%
Suspension 100%
Time to SS = 3-5 wk

Elderly (60-79 y)
Vmax = 5.5 mg/kg/d
Km = 5.8 mg/L

Adults (19-64 y)
Vmax = 8.45 mg/kg/d
Km = 6.25 mg/L

Effect of Age on Total Plasma Valproate Concentrations

6 young, 6 elderly volunteers—400 mg dose

Effect of Age on Unbound VPA Concentrations

Unbound Plasma Valproate Concentrations

Free Fraction

6%

11%

### Pharmacokinetics of Newer AEDs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Absorption</th>
<th>Binding</th>
<th>Elimination†</th>
<th>T&lt;sub&gt;1/2&lt;/sub&gt; (hr)</th>
<th>Interactions*</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBP</td>
<td>≤60%‡</td>
<td>0%</td>
<td>100% renal</td>
<td>5-9</td>
<td>No</td>
</tr>
<tr>
<td>LTG</td>
<td>100%</td>
<td>55%</td>
<td>100% hepatic</td>
<td>18-30</td>
<td>Uni-D</td>
</tr>
<tr>
<td>LVT</td>
<td>~100%</td>
<td>&lt;10%</td>
<td>66% renal</td>
<td>4-8</td>
<td>No</td>
</tr>
<tr>
<td>OXC/MHD§</td>
<td>100%</td>
<td>40%</td>
<td>100% hepatic</td>
<td>5-11</td>
<td>Bi-D</td>
</tr>
<tr>
<td>PGB</td>
<td>90%</td>
<td>0%</td>
<td>100% renal</td>
<td>5-7</td>
<td>No</td>
</tr>
<tr>
<td>TGB</td>
<td>~100%</td>
<td>96%</td>
<td>100% hepatic</td>
<td>5-13</td>
<td>Yes</td>
</tr>
<tr>
<td>TPM</td>
<td>≥80%</td>
<td>15%</td>
<td>30%-55% renal</td>
<td>20-30</td>
<td>Bi-D</td>
</tr>
<tr>
<td>ZNS</td>
<td>80%-100%</td>
<td>40%-60%</td>
<td>50%-70% hepatic</td>
<td>50-80</td>
<td>Uni-D</td>
</tr>
</tbody>
</table>

†In noninduced adult; ‡Saturable; §Binding, elimination, and t<sub>1/2</sub> refer to MHD; *Bi-D=bidirectional; Uni-D=unidirectional.

Adapted from Cloyd JC, Remmel RP. *Pharmacotherapy*. 2000;20:139S-151S.
Effect of CBZ on Serum Simvastatin and Simvastatin Acid Concentrations

Ucar et al, EJCP, 2004
Effect of Grapefruit Juice on Drug Metabolism
Inhibition of CYP 3A4 by Grapefruit Juice: Effect on Carbamazepine Serum Levels

Potent inducer of CYP 3A enzymes
Herbs and Epilepsy

• Herbs may increase the risk for seizures:
  – intrinsic proconvulsant properties
  – contamination by heavy metals
  – effects on the cytochrome P450 enzymes and P-glycoproteins,
  – herb–drug interactions
<table>
<thead>
<tr>
<th>Herbs</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>With neurotoxic components</strong></td>
<td></td>
</tr>
<tr>
<td>Ephedra (ma huang)</td>
<td>Ephedra alkaloids can induce seizures, as well as predispose patients to both hemorrhagic and ischemic stroke (Bruno et al., 1993)</td>
</tr>
<tr>
<td>Evening primrose oil</td>
<td>γ-linoleic acid (GLA) reduces seizure threshold</td>
</tr>
<tr>
<td>Ginkgo Biloba</td>
<td>4′-O-methoxypridoxine (&quot;Ginkgotoxin&quot;) found in seeds and leaves</td>
</tr>
<tr>
<td>Pennyroyal</td>
<td>(R)-(+)–pulegone induces seizures.</td>
</tr>
<tr>
<td>Star anise – Japanese (<em>Illicium anisatum</em>)</td>
<td>Anisatin is a known neurotoxin</td>
</tr>
<tr>
<td>Star anise – Chinese (<em>Illicium verum</em>)</td>
<td>Veansatins A, B, C are neurotoxic at high doses; herb may be contaminated with anisatin.</td>
</tr>
<tr>
<td>Star fruit (<em>averrhoa carambola</em>)</td>
<td>Oxalate compound increases GABA uptake in the cerebral cortex of the rat (Neto et al., 1998; Fang et al., 2007)</td>
</tr>
<tr>
<td>Wormwood (<em>artemesia absinthium</em>)</td>
<td>Terpene thuojone found in a number of herbs (Spinella, 2001)</td>
</tr>
<tr>
<td><strong>Altering AED disposition</strong></td>
<td></td>
</tr>
<tr>
<td>Ginkgo biloba</td>
<td>Induces CYP2C19, reducing serum levels of phenytoin and valproate</td>
</tr>
<tr>
<td>Saint John’s wort (<em>Hypericum perforatum</em>)</td>
<td>Inhibits CYP enzymes, induces intestinal Pgp; no effect on carbamazepine levels</td>
</tr>
<tr>
<td>Grapefruit</td>
<td>Inhibits CYP 3A activity; increases bioavailability of carbamazepine and diazepam</td>
</tr>
<tr>
<td>Shankhpushpi (ayurveda)</td>
<td>Decreased activity and serum levels of phenytoin</td>
</tr>
<tr>
<td>Sho-seiryu-to/sho saiko -to</td>
<td>Delayed gastric emptying in rats led to increased carbamazepine levels</td>
</tr>
</tbody>
</table>
Epilepsy Treatment in the Elderly

• Monotherapy is possible for 90%+ of patients.
• Typical nursing home patient is on 6-8 medications.
• Choose AEDs with minimal interactions
  – e.g. levetiracetam, pregabalin and gabapentin
• Titrate slowly
• Avoid older AEDs with strong induction effects (phenytoin, phenobarbital, and carbamazepine)
• Avoid newer AEDs with established adverse cognitive effects (topiramate and zonisamide)
Topiramate and Zonisamide

• 94% of patients experienced cognitive viscosity with either drug as an adjunctive agent*
• 63% of the patients were unaware of the effect*

Oxcarbazepine and Tiagabine

- Oxcarbazepine can result in hyponatremia much more commonly in elderly
- Tiagabine has been associated with encephalopathy
Older AEDs and the Elderly

- Inducing drugs: phenytoin, carbamazepine and phenobarbital – result in consequences
  - Behavioral
  - Cognitive
- Valproate - weight gain, risk of encephalopathy. Can be used, but carefully.
- Phenobarbitol can have significant cognitive slowing, depression, or other behavioral consequences
80% of 21,435 pts. received phenobarbital or phenytoin.
Most patients were taking phenytoin
18.9% of patients with previously diagnosed epilepsy
9.4% of patients with newly diagnosed epilepsy received phenobarbital
   White veterans
   Patients receiving neurology consultation were half as likely to receive phenytoin monotherapy.

Epilepsy in long term care patients

- Not rare
- Demographics different than normal intelligence people
- Often misdiagnosed
- Can be treated with monotherapy
- Side effects are more common
- Use new seizure medications
Questions & Answers
Thank you for your attention.