Management of epilepsy

Dr. Sanjib Sinha

Professor of Neurology

NIMHANS, Bengaluru

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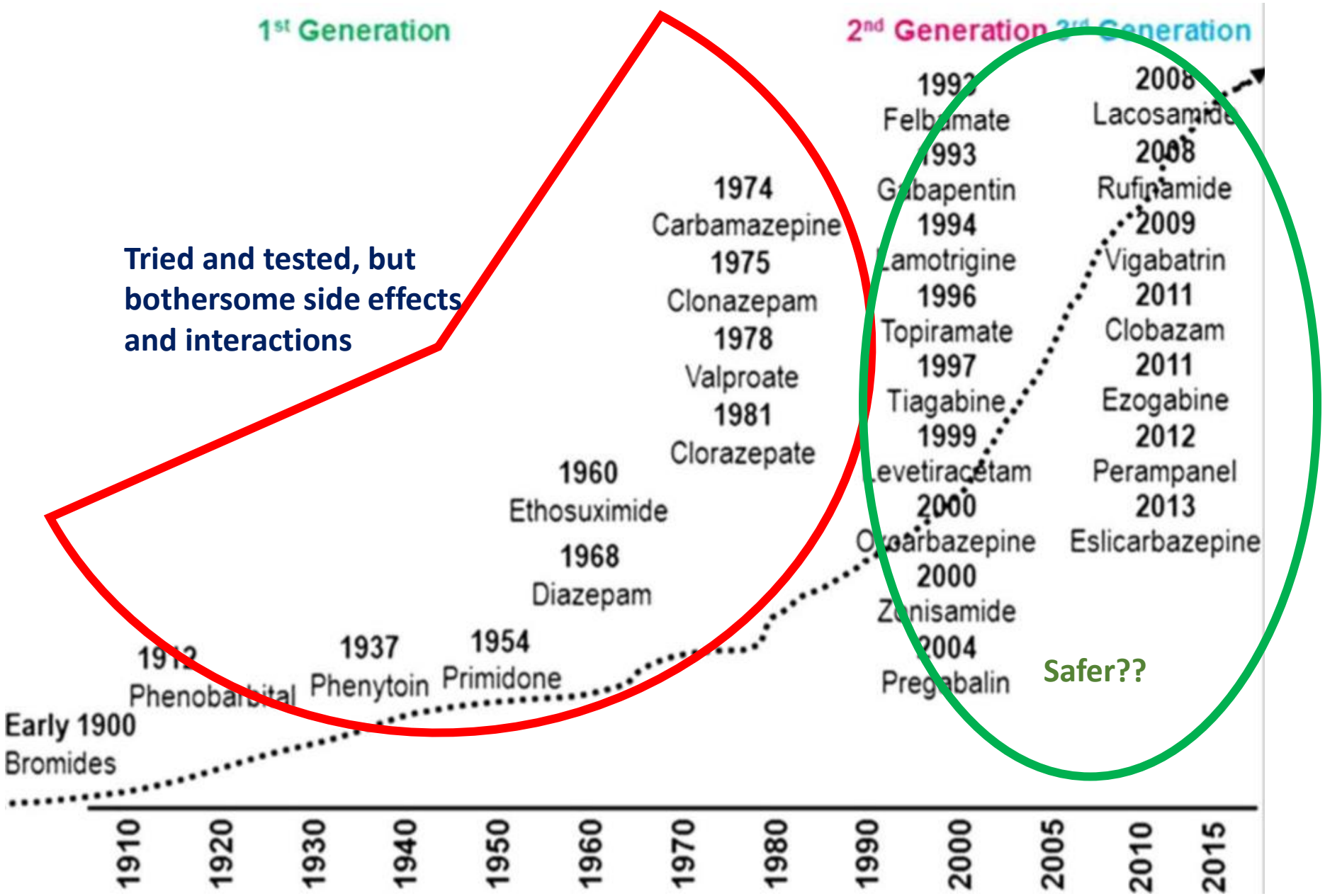
Steps in the management of a patient with epilepsy

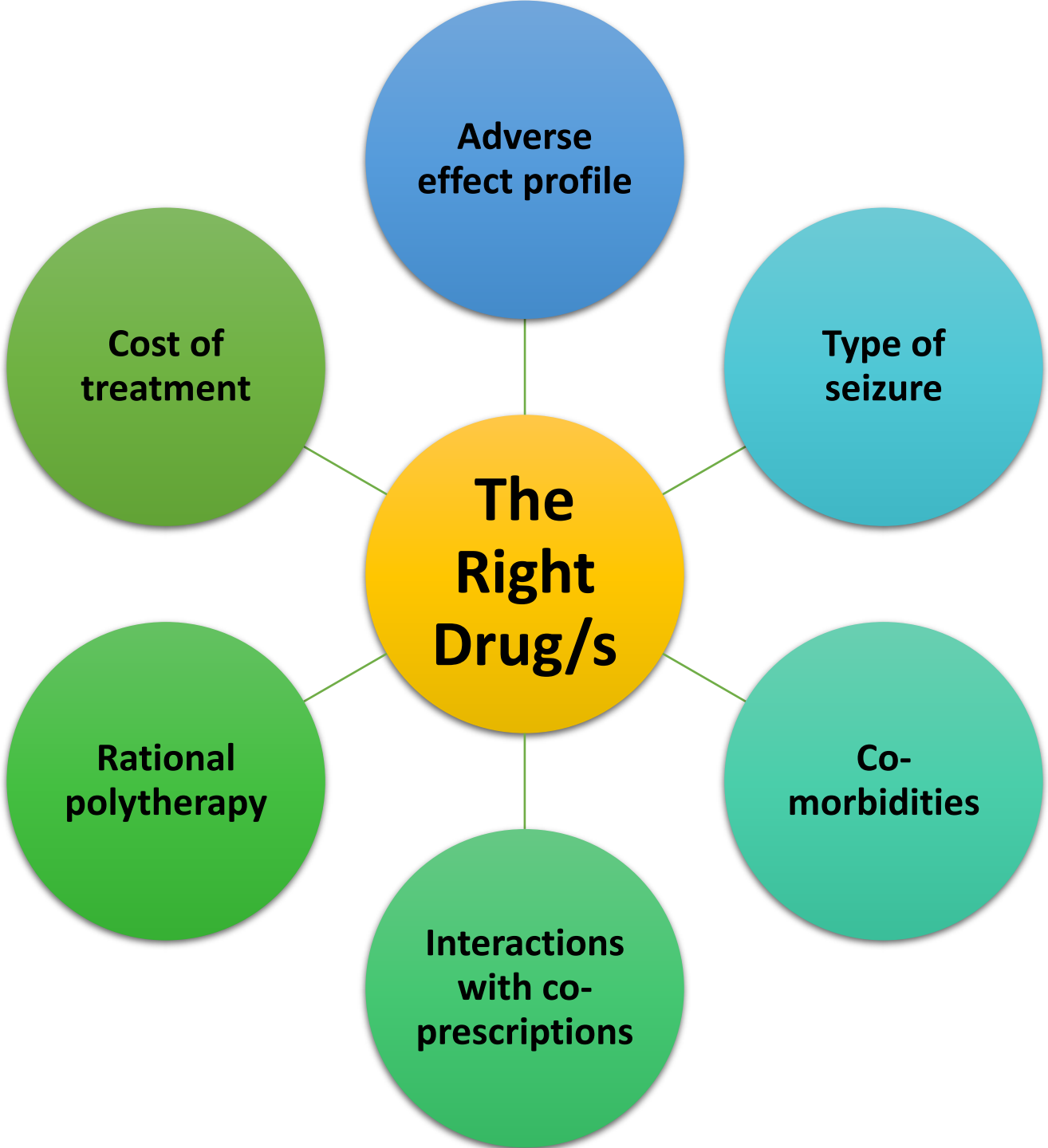
- **Clinical examination**
- **Investigations (Imaging/EEG)**
- **Choosing the right drug and the right dose**
- **Monitoring for side effects, ensure compliance**
- **Tapering of drugs – if possible**

Treatment for epilepsy

- The treatment of epilepsy is based on the cause.
- The preliminary treatment is to start the patient on the appropriate medicine i.e. anti-seizure medication.
- Up-to 60% of people will obtain control of seizures with one or more drugs but some go on to develop ‘refractory/drug resistant epilepsy’
- These are epilepsies which are not controlled even with 2 or more appropriate drugs tried for an optimal period of time.
- These patients include those with structural abnormalities in the brain such as tumors, hippocampal sclerosis or developmental malformations of the brain architecture.

Many drugs – what to choose????




Adverse effect profile
Cost of treatment
Type of seizure
The Right Drug/s
Rational polytherapy
Co-morbidities
Interactions with co-prescriptions

ILAE: Recommendations of Anti-Seizure Medications

Seizure type or epilepsy syndrome	studies	studies	studies	(in alphabetical order)
Adults with partial-onset seizures	4	1	34	Level A: CBZ, LEV, PHT, ZNS Level B: VPA Level C: GBP, LTG, OXC, PB, TPM, VGB Level D: CZP, PRM
Children with partial-onset seizures	1	0	19	Level A: OXC Level B: None Level C: CBZ, PB, PHT, TPM, VPA, VGB Level D: CLB, CZP, LTG, ZNS
Elderly adults with partial-onset seizures	1	1	3	Level A: GBP, LTG Level B: None Level C: CBZ Level D: TPM, VPA
Adults with generalized onset tonic–clonic seizures	0	0	27	Level A: None Level B: None Level C: CBZ, LTG, OXC, PB, PHT, TPM, VPA Level D: GBP, LEV, VGB
Children with generalized-onset tonic–clonic seizures	0	0	14	Level A: None Level B: None Level C: CBZ, PB, PHT, TPM, VPA Level D: OXC
Children with absence seizures	1	0	7	Level A: ESM, VPA Level B: None Level C: LTG Level D: None
Benign epilepsy with centrotemporal spikes (BECTS)	0	0	3	Level A: None Level B: None Level C: CBZ, VPA Level D: GBP, LEV, OXC, STM
Juvenile myoclonic epilepsy (JME)	0	0	1	Level A: None Level B: None Level C: None Level D: TPM, VPA

Glauser et al. Epilepsia 2013; 1-13

Questions to ask before starting treatment

- Is it a seizure?
- Is it really the first seizure?
- Are there risk factors for a second seizure?
- Should the person be allowed to drive?
- Should there be limitations on work?
- What are the risks of not treating?
- What are the risks of treating?

Treatment Gap in India!

Treatment gap

- Medical: Epilepsy treatment gap in India ranges from 22% among urban, middle-income people to 90% in villages
- Surgical: A survey conducted by the International League Against Epilepsy, International Bureau of Epilepsy, and World Health Organization in 2006 found that epilepsy surgery was available in only 13% of LAMIC compared with 66% of high-income countries
- The gap is reported to be influenced by various factors:
  - lack of access to or knowledge of ASMs, poverty, cultural beliefs, stigma, poor health delivery infrastructure, & shortage of trained professionals

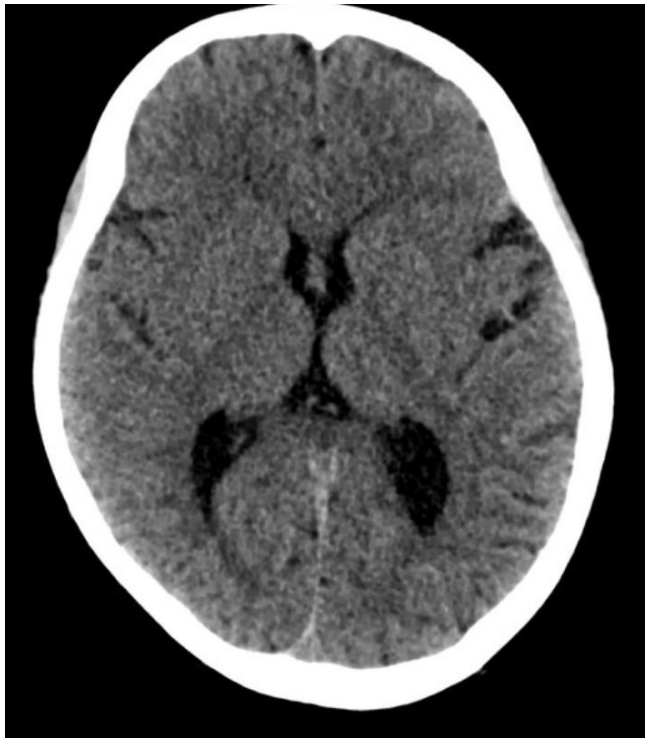
40-year-old suffered from a head injury in a RTA. One hour later he had one episode of seizure lasting 1 minute.

Q1. This patient has epilepsy

- Yes
- No

Q2. This patient needs long term ASM

- Yes
- No



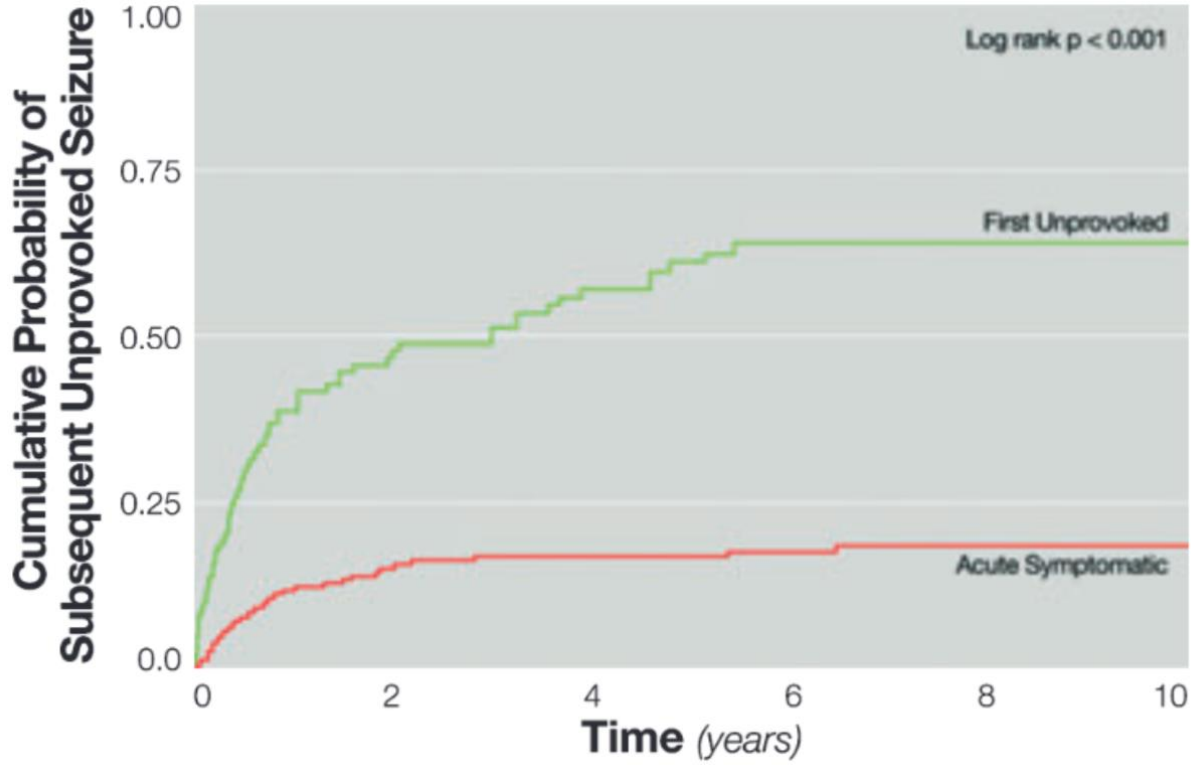
Epilepsia, 50(5):1102–1108, 2009
doi: 10.1111/j.1528-1167.2008.01945.x

FULL-LENGTH ORIGINAL RESEARCH

Is a first acute symptomatic seizure epilepsy? Mortality and risk for recurrent seizure

*Dale C. Hesdorffer, †Emma K. T. Benn, ‡Gregory D. Cascino, and §¶W. Allen Hauser

- Acute symptomatic seizures may occur following traumatic brain injuries, strokes and metabolic derangements
- If brain damage is not significant, patient may need ASMs for only a short duration (weeks-months). Does NOT need long term ASM therapy



2.5-year-old brought by mother with high grade fever since morning and one episode of generalized seizure in the afternoon. Child is otherwise conscious, no meningeal signs and has no neurological deficits/developmental delay. History of similar episode 6 months ago

Q1. Does this child need extensive evaluation?

- Yes
- No

Q2. Does this child need to be started on anti-seizure medication?

- Yes
- No

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

FROM THE AMERICAN ACADEMY OF PEDIATRICS

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

Clinical Practice Guideline—Febrile Seizures: Guideline for the Neurodiagnostic Evaluation of the Child With a Simple Febrile Seizure

When the diagnosis of simple FS is considered – Neuroimaging/EEG is NOT recommended

If meningitis is suspected – LP may be done

Treatment of FS-

a. Immediate treatment of fever
b. Clobazam prophylaxis (0.3-1mg/kg/day - <5kg – 5mg/d 5-10kg – 10mg/d and >10kg-15mg/day)

When to refer to higher center

a. Associated developmental delay/regression
b. Focal deficit after seizure
c. Status epilepticus

When a child presents with febrile status epilepticus – AVOID SODIUM CHANNEL BLOCKERS

A young man with the first episode of unknown onset tonic clonic seizure 1 day ago

- Q1. Do you think brain imaging is necessary for this patient
  - Yes
  - No

- Q2. Do you need an EEG for this patient?
  - Yes
  - No

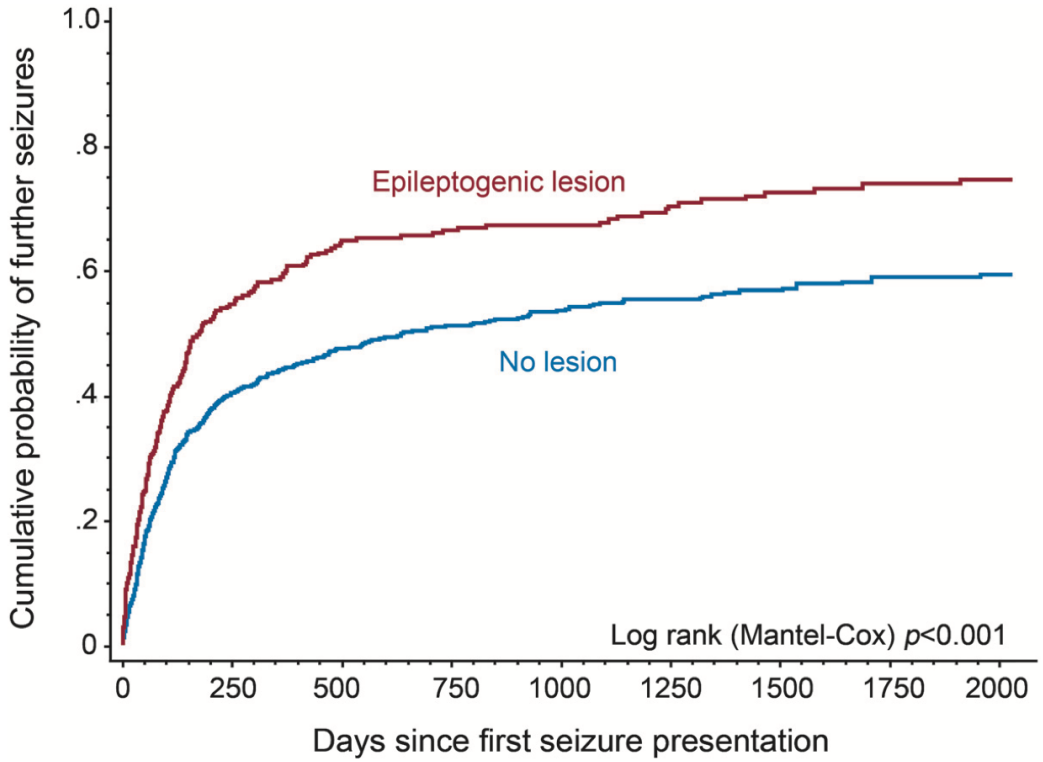
MRI is superior to CT in detecting-

a. Mesial temporal sclerosis
b. Small cortical malformations
c. Small cavernomas

Neuroimaging of first-ever seizure

Contribution of MRI if CT is normal

Cumulative probability of second seizure for epileptogenic lesion on any neuroimaging (CT or MRI)



What this graph tells us –

a. The probability of a second seizure is HIGH (>60%) if an epileptogenic lesion is detected on CT/MRI

b. Therefore imaging is useful to predict seizure recurrence

If MRI is available/affordable – better to do MRI rather than CT

Common indications for EEG in Epilepsy

- **After 1st episode if considering the possibility of IGE syndrome/JME - Classical EEG findings can help make the diagnosis of epilepsy even after 1st seizure**
- **In typical childhood absence**
- **When patient is not responding to drugs**
- **Patient having a prolonged post ictal phase**
- **In childhood epilepsies, especially when there is co-existing developmental delay/regression of milestones**

Factors that are associated with heightened risk of seizure recurrence

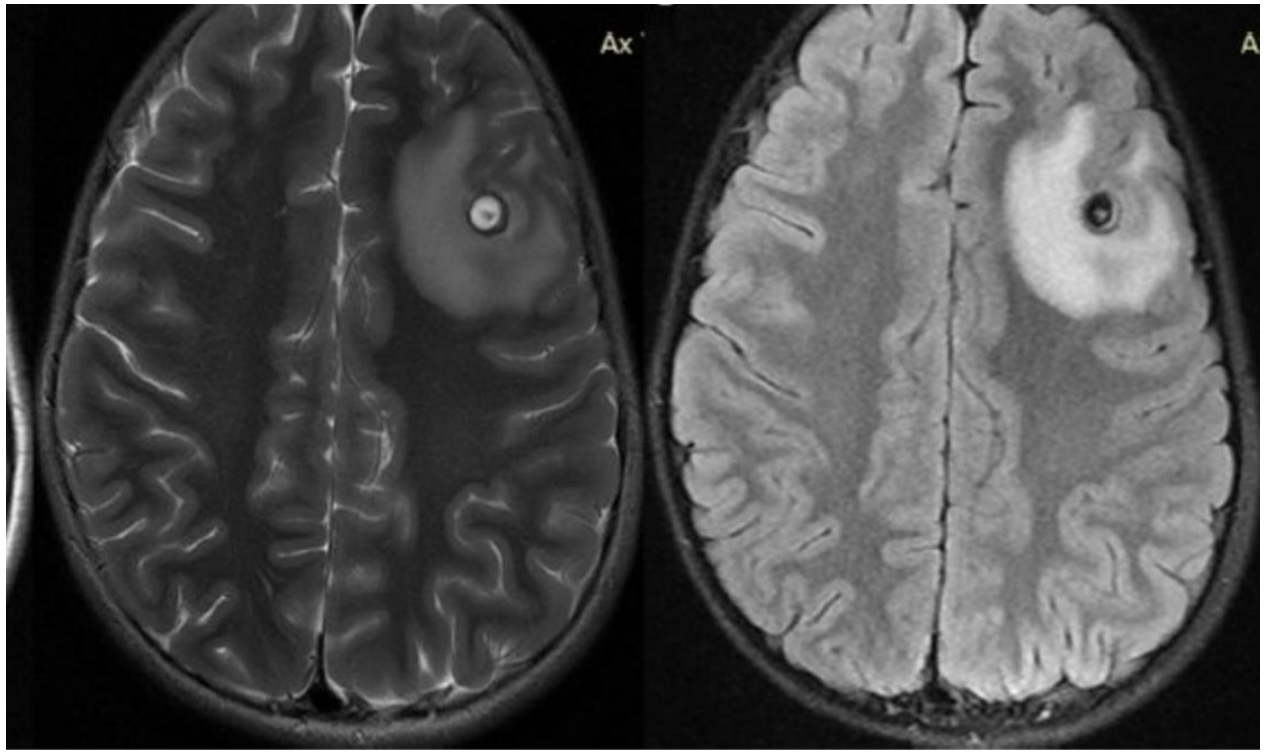
- **Potentially epileptogenic lesions on imaging (e.g. gliosis)**
- **Focal neurological findings**
- **Focal seizure phenomenology (including Todd's paresis)**
- **Focal or generalised epileptiform activity on EEG**
- **Tumours or other progressive lesions as the underlying pathology**
- **New onset Status epilepticus (NOSE)**
- **Family history of epilepsy**

Other Investigations after the first episode of seizure

- Hemogram, renal and liver function tests, blood sugar and calcium are tests the are recommended for patients who have had a recent seizure
- CSF – if inflammatory/infectious diseases of the brain are being considered
- The information gained may help in-
  - Inferring if it was an acute symptomatic seizure (e.g. if low sodium levels were identified)
  - To avoid certain anti seizure medications (e.g. avoiding valproate when there is liver injury)
  - As a baseline measure – for monitoring ASM side effects

The earlier patient has come back with his scan (see picture below). What would you do?

1. Not start ASM
2. Start ATT
3. Start ASM and ophthalmology evaluation



Neurocysticercosis and epilepsy

- NCC is one of the most common causes of symptomatic epilepsy in India
- When the cyst has got calcified there is no role for any anti-helminthic therapy.
- Viable NCC (when few in number) and not intraventricular/ocular : can be treated with anti-helminthic drugs + steroids (to reduce inflammatory side effects that occur when the cyst degenerates)
- If the cyst is no longer visualized in follow up imaging (in about 6 months), ASMs may be tapered and stopped

Choosing Anti-Seizure Medications

Focal onset seizures

Old ASMs

- Carbamazepine
- Phenytoin
- Phenobarbitone

New ASMs

- Lacosamide
- Oxcarbazepine
- Lamotrigine
- Levetiracetam/ Brivaracetam
- Perampanel
- Clobazam
- Zonisamide
- Topiramate

Choosing Anti-Seizure Medications

Generalised/unkown onset seizures

Old ASMs

- Valproate
- Phenobarbitone

New ASMs

- Levetiracetam/ Brivaracetam
- Lamotrigine
- Perampanel
- Zonisamide
- Topiramate

19-year-old lady with early morning myoclonus and GTCS (4 episodes so far)

- What drug will you choose?

1. Valproate
2. Levetiracetam
3. Phenobarbitone
4. Carbamazepine

Challenges & Solutions
1. Treatment Option:

- The most effective antiseizure medication (ASM) in generalized epilepsies is sodium valproate.*
- However, this drug is best avoided in young women of childbearing age, as it can cause polycystic ovarian syndrome, weight gain and hair loss.
- Men & women without child bearing potential: Valproate
- Also valproate is the ASM which is associated with the highest risk of major congenital malformation (8.9 %), and should be avoided in this particular group of patients.

** Marson AG et al. The SANAD study of effectiveness of valproate, lamotrigine or topiramate for generalized and unclassifiable epilepsy: an unblinded randomised controlled trial. Lancet 2007:369:1016-26.*

Drugs for women with epilepsy and IGE syndromes

- **In women in the reproductive age group – AVOID SODIUM VALPROATE**
- **There is strong evidence for teratogenicity even at relatively low doses**
- **Also interferes with menstrual functions, can cause weight gain, hair loss and acne**
- **If a lady is on valproate, refer to make the switch to an alternative drug**
- **Levetiracetam and lamotrigine are ideal for women in the reproductive age group**

Drugs that can be used in IGE:

a. Sodium Valproate (for men)
b. Levetiracetam
c. Lamotrigine (does not help for myoclonic jerks)
d. Zonisamide
e. Phenobarbitone

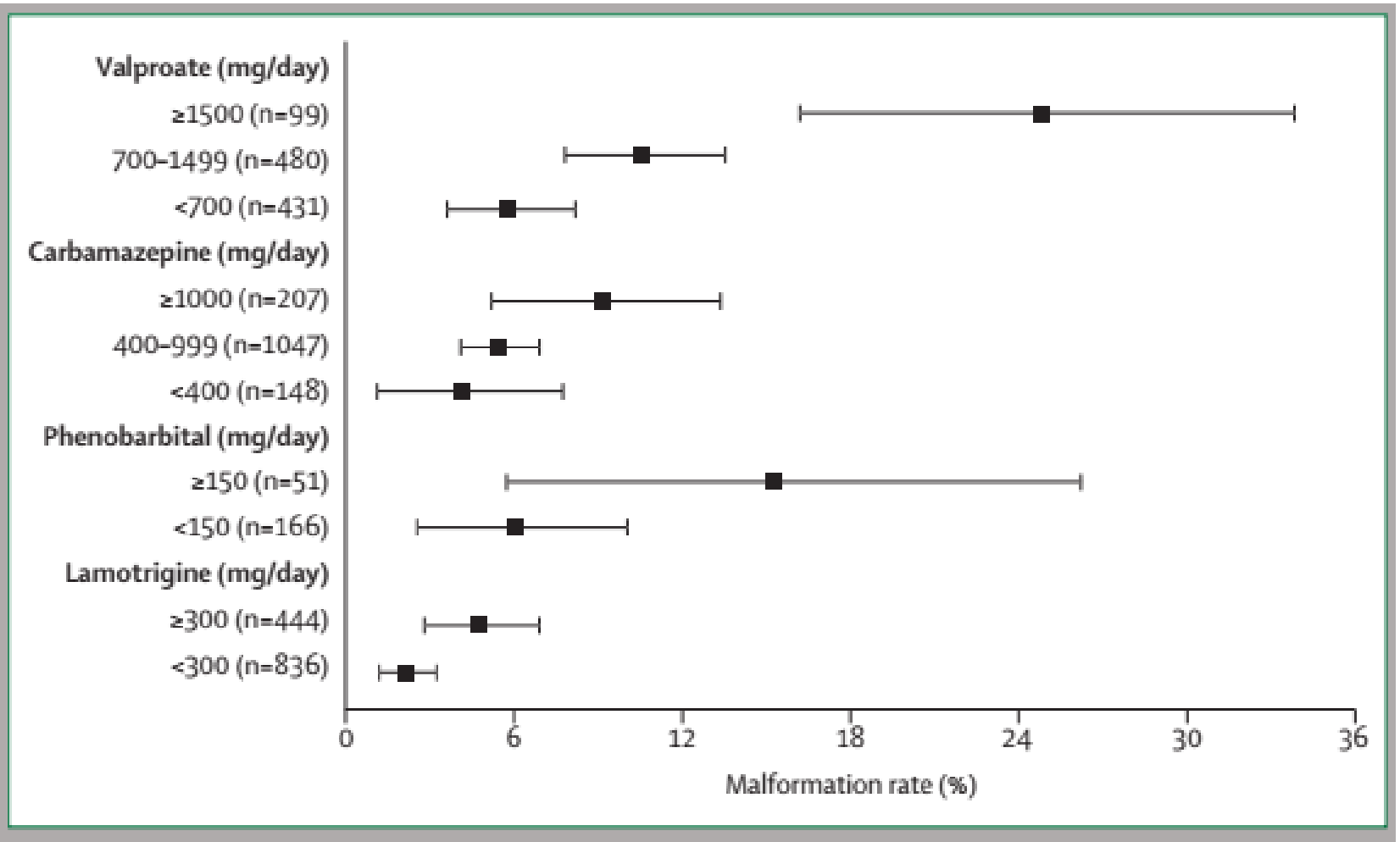
Drugs that are to be avoided in IGE:

a. Carbamazepine
b. Phenytoin

23-year-old married lady with epilepsy on phenobarbitone wishes to conceive. Last seizure was 6 months ago. What will be your plan?

1. Reduce dose of phenobarbitone and add folic acid
2. Replace phenobarbitone with levetiracetam and start folic acid after conception
3. Add another drug (levetiracetam) and continue phenobarbitone
4. Stop Phenobarbitone
5. Replace with levetiracetam and start folic acid at least 3-4 months before conception

Drugs and pregnancy – global evidence point to lower risk of MCM with LTG and LEV



Registries	Monotherapy (%)	Polytherapy (%)
UK registry	4.5	8.6
North America registry	3.7	6
Kerala registry	6.4	9.9

Evidence from India - Kerala Registry of Epilepsy and Pregnancy (KREP)

- 1,688 fetuses in resulting in 1,622 live births till 1 year of life.
- The MCM rate for all live births was 6.84% and for all pregnancy outcomes including fetal loss was 7.11%.
- Monotherapy: 6.4%, Polytherapy: 9.9%;
- WWE not on antiepileptic drugs: 5.6%
- Women without epilepsy or AED exposure 3.45%
- MCM Clobazam monotherapy 22% (n 9), need to be further evaluated.

Some tenets for treatment:

Switch to safer ASM, start folic acid preconceptionally, advice close follow up with obstetrician in pregnancy, counsel regarding effect of drug and epilepsy on pregnancy, refer to neurologist

Thomas, Sanjeev V et al. "Malformation risk of antiepileptic drug exposure during pregnancy in women with epilepsy: Results from a pregnancy registry in South India." Epilepsiavol. 58,2 (2017): 274-281. doi:10.1111/epi.13632

24-year-old lady, 5 months pregnant on levetiracetam (18mg/kg/day) presented with seizure recurrence.

Q1. How will you treat this patient?

- Add another drug
- Increase Levetiracetam dose
- Continue the same

Epilepsia, **48**(6):1111–1116, 2007
Blackwell Publishing, Inc.

Pharmacokinetics of Levetiracetam during Pregnancy, Delivery, in the Neonatal Period, and Lactation

*Torbjörn Tomson, †Ragnar Palm, ‡Kristina Källén, §Elinor Ben-Menachem, ¶Birgitta Söderfeldt, **Bo Danielsson, ††Rune Johansson, ‡‡Gerhard Luef, and §§Inger Öhman

Pregnancy increases clearance of levetiracetam. It may not necessarily result in poor therapeutic effect (evidence regarding this is still unclear)

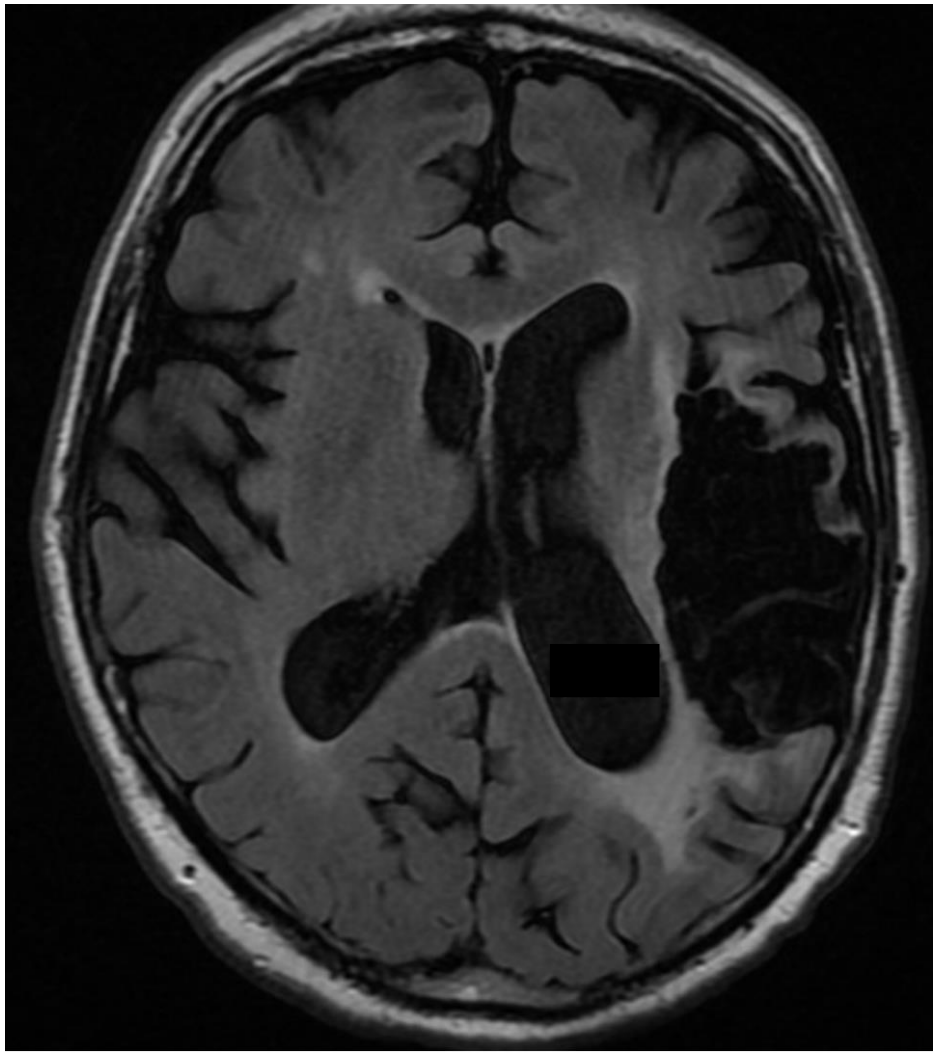
Dose modification may be needed for certain patients, especially if there is a recurrence

In the previous case, dose of LEV probably needs to be increased to ~25mg/kg

65-year-old with history of stroke 2 years ago. Has come with 4 episodes of right focal seizures with

- What is the drug you would avoid in this patient?

1. Carbamazepine
2. Lamotrigine
3. Lacosamide
4. Levetiracetam



Treatment Challenges:

- What factors need to be kept in mid while prescribing the anti-seizure medication?
- What are the drugs of choice in this patient?

Factors to be borne in mind while prescribing ASMs:

- There are three relevant issues in the treatment of epilepsy for the elderly:
- Changes in pharmacokinetic parameters,
- Polytherapy is likely and often unavoidable (including non-ASMs), and
- Susceptibility to adverse drug effects.

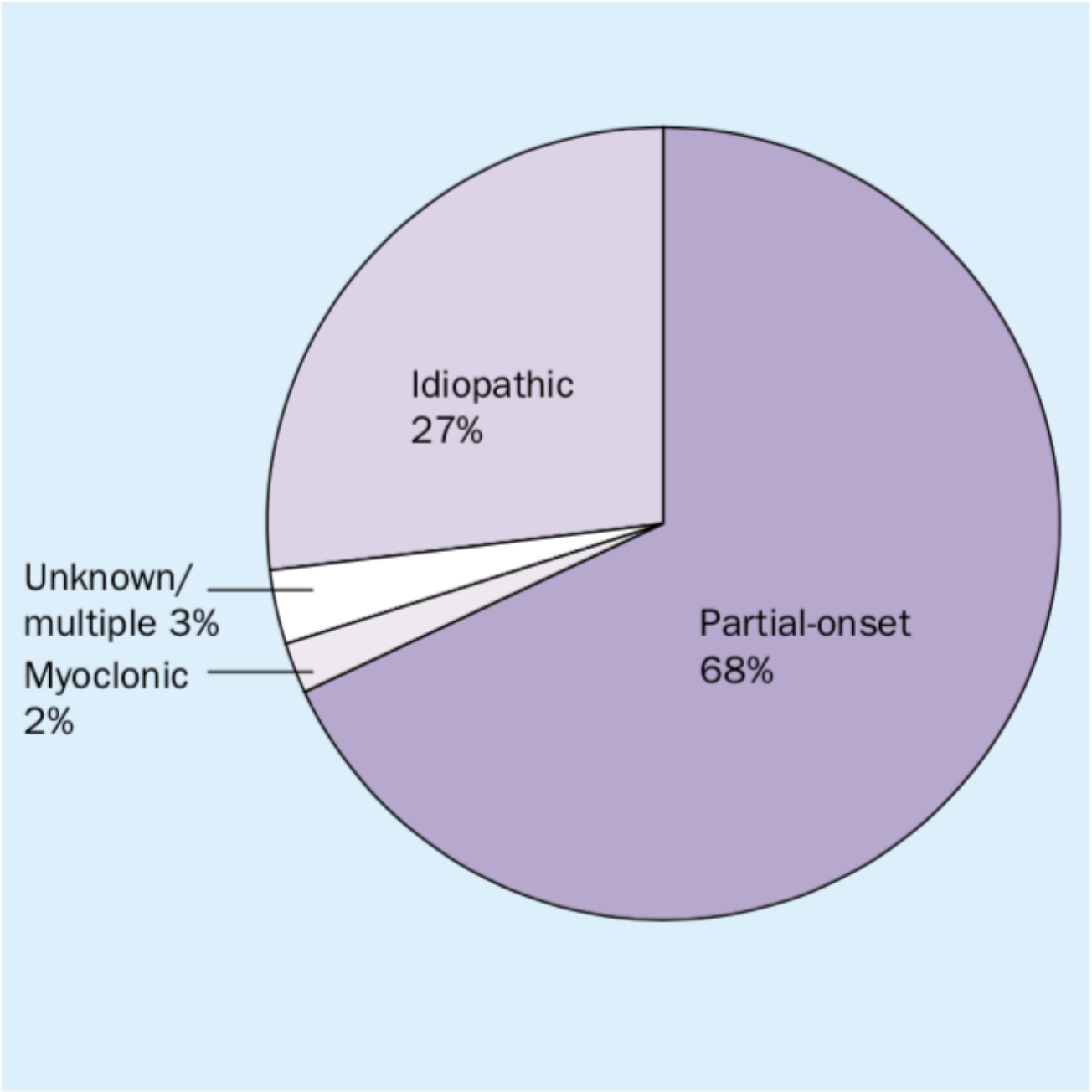
ASMs and hyponatremia

- **Hyponatremia is the commonest electrolyte abnormality seen in elderly and an independent risk factor for mortality.**
- **Emphasizes the need to use the antiepileptic with least potential to cause hyponatremia.**
- **Oxcarbazepine and carbamazepine have been particularly associated with a risk of hyponatremia**
- **Eslicarbazepine too is not safe in patients with history of CBZ induced hyponatremia**

Kaur et al. Antiepileptic drug therapy in the elderly: a clinical pharmacological review

- **Most new seizures in elderly patients are partial in onset with or without secondary generalisation**
- **10-30% can present with status epilepticus**
- **Cerebrovascular disease is the single most important cause of seizures and epilepsy in the elderly**
- **More often, infarcts are cortical and hemorrhagic. Subcortical small infarcts and small vessel disease are less likely to cause seizures**

	Frequency (%)
Acute symptomatic	
Acute cerebral infarction	3–43
Head injury	17
Subarachnoid haemorrhage	8–24
Intracranial haemorrhage	8
Subdural haematoma	1
Metabolic distrubance	6–21
Alcohol withdrawal/drug related	10
Remote symptomatic	
Previous cerebral infarction	3–9
Head injury	2–21
Cerebral atrophy	5–13
Tumour	8–45
Cerebrovascular disease	49
Non-vascular dementia	9–17



Effects on cognition

- Older antiepileptics including **PB**,PHT >VPA,CBZ have been linked to cognitive impairment in various age groups.
- Phenytoin has been linked to disturbances in attention, visuomotor function, and mental speed, though overall effect is small
- Among newer antiepileptics, **topiramate** has been shown to negatively affect cognitive domains **(mainly language)** in nearly 10% patients
- Lamotrigine and levetiracetam are virtually free of cognitive side effects
- Polytherapy increases risk of cognitive worsening in the elderly

In the same elderly patient, would you also prescribe vitamin D/calcium?

- Yes
- No

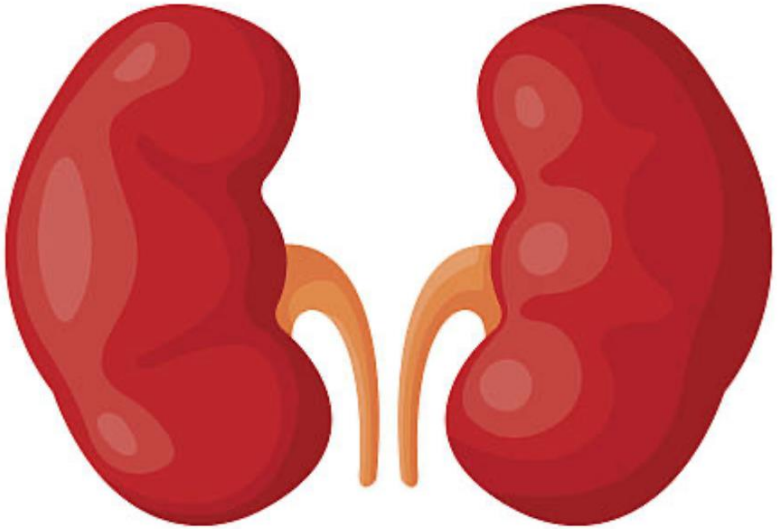
- **Epilepsy can lead to falls and fractures, particularly in elderly.**
- **Annual measurement of Calcium, Phosphorous and ALP is recommended**
- **Daily calcium (1-1.5g) with VitD supplementation (1000U/d)**
- **When on enzyme inducers, can increase dose up to 4000U/d**
- **No guidelines available for administration of bisphosphonates/hormone replacement while on AEDs to prevent osteoporosis**

Mechanisms of disruption of bone health

- **Increased VitD and K metabolism**
- **Decrease intestinal calcium absorption**
- **Inhibition of IGF**
- **Suppression of osteoblasts (Valproate)**
- **Acceleration of bone loss (Gabapentin)**

50 year old with chronic kidney disease (GFR = 20ml/h) also has epilepsy. You plan on starting levetiracetam.
Is dose adjustment required?

- Yes
- No



ASMs in patients with CKD

- **The use of ASM in patients with renal failure is complex.**

Drug	GFR 30-59	15-29	<15	HD
GABAPENTIN	Up to 1400mg/d	Up to 700mg/d	Up to 300mg/d	100% of daily dose after HD
LAC	Up to 300mg/d	Up to 300mg/d	Up to 300mg/d	50% post HD supplement
LEV	50% dose reduction	50% dose reduction	50% dose reduction	50% post HD supplement
OXC	50% dose reduction	50% dose reduction	50% dose reduction	Insufficient data
TOP	50% dose reduction	50% dose reduction	50% dose reduction	50% post HD supplement
ZON	No adjustment	Use with caution, no data	Use with caution, no data	Use with caution, no data

Clearance with dialysis

Low molecular size
High water solubility
Low protein binding
Low volume of distribution
High flux, large pore membranes

High molecular size
Low water solubility
High protein binding
High volume of distribution
Membranes with small pores

No adjustsments in CKD

BRIV
CBZ
CLOB
VPA

Summary of advantages of various ASMs: Useful for selecting it!

No cognitive effects	No weight gain	Linear kinetics	Minimal protein binding	Rapid titration	No/minimal neuropsychiatric symptom
OXC LTG LEV VPA,CBZ (minimum)	PHT OXC LTG	OXC LTG LEV	LEV TOP GABAPENTIN PREGABALIN	LEV PREGABALIN GABAPENTIN	LTG VPA ZON

8-year-old girl presented with childhood absence epilepsy. What is your drug of choice?

1. Levetiracetam
2. Ethosuximide
3. Lacosamide
4. Carbamazepine

Treatment of Childhood absence epilepsy

- 1st line – Ethosuximide (T-type calcium channel blocker)
  - Monitor blood counts periodically and ethosuximide can cause bone marrow suppression rarely
- If not available use sodium valproate.

Sodium channel blockers can worsen absence. Levetiracetam is not very useful

Pediatric Drugs (2019) 21:15–24
https://doi.org/10.1007/s40272-019-00325-x

THERAPY IN PRACTICE

A Practical Guide to Treatment of Childhood Absence Epilepsy

Sudha Kilaru Kessler[1] · Emily McGinnis[2]

Published online: 8 February 2019

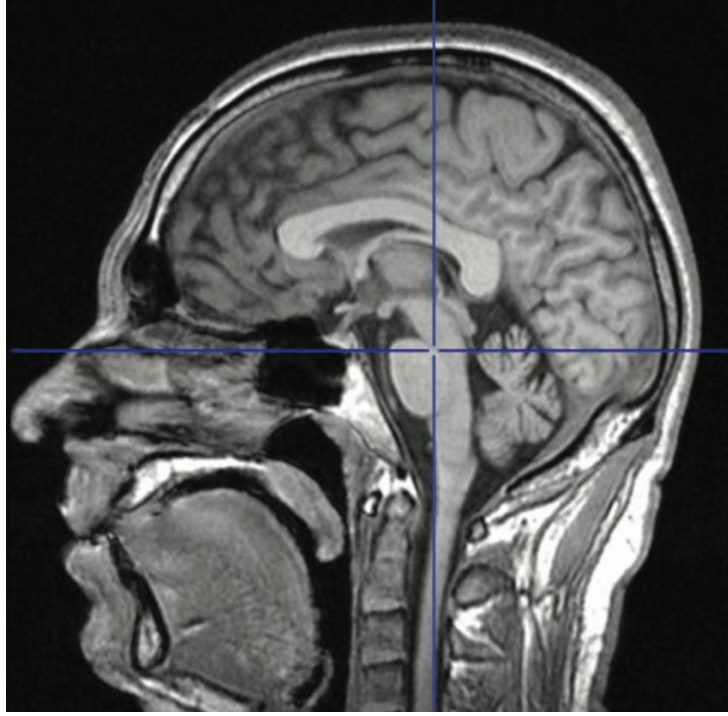
Name	Initial dose	Maintenance dose	Maximum dose
Ethosuximide	10–15 mg/kg/day	20–30 mg/kg/day	40 mg/kg/day up to 2 g/day
Valproate	10–15 mg/kg/day	20–30 mg/kg/day	60 mg/kg/day up to 3 g/day
Lamotrigine	For patients not taking valproate or other enzyme inducers: 0.3 mg/kg/day For patients taking valproate: 0.15 mg/kg/day For patients taking enzyme inducers and NOT valproate: 0.6 mg/kg/day	For patients not taking valproate or other enzyme inducers: 4.5–7.5 mg/kg/day For patients taking valproate: 1–5 mg/kg/day For patients taking enzyme inducers and NOT valproate: 5–15 mg/kg/day	For patients not taking valproate or other enzyme inducers: 300 mg/day For patients taking valproate: 200 mg/day For patients taking enzyme inducers and NOT valproate: 400 mg/day
Clobazam	<30 kg: 5 mg/day >30 kg: 10 mg/day	<30 kg: 10–20 mg/day >30 kg: 40 mg/day	<30 kg: 40 mg/day >30 kg: 60–80 mg/day
Levetiracetam	20–30 mg/kg/day	40 mg/kg/day	60–90 mg/kg/day up to 3 g/day
Topiramate	1–3 mg/kg/day	5–9 mg/kg/day	15 mg/kg/day up to 1600 mg/day
Zonisamide	1–2 mg/kg/day	5–8 mg/kg/day	12 mg/kg/day up to 1 g/day

A 20-year-old male on phenytoin presents with acute onset of giddiness and imbalance while walking with slurring of speech. What is the next step in his evaluation?

1. Urgent neuroimaging
2. Serum phenytoin levels

ASMs causing cerebellar dysfunction

- **The exact mechanism behind cerebellar dysfunction due to ASMs is not clear for many of the drugs**
- **Drugs such as phenytoin are toxic to the Purkinje cells of the cerebellum**
- **Ion channel dysfunction is another hypothesized cause**



Drugs that can cause ataxia

Any ASM can but the common ones are-

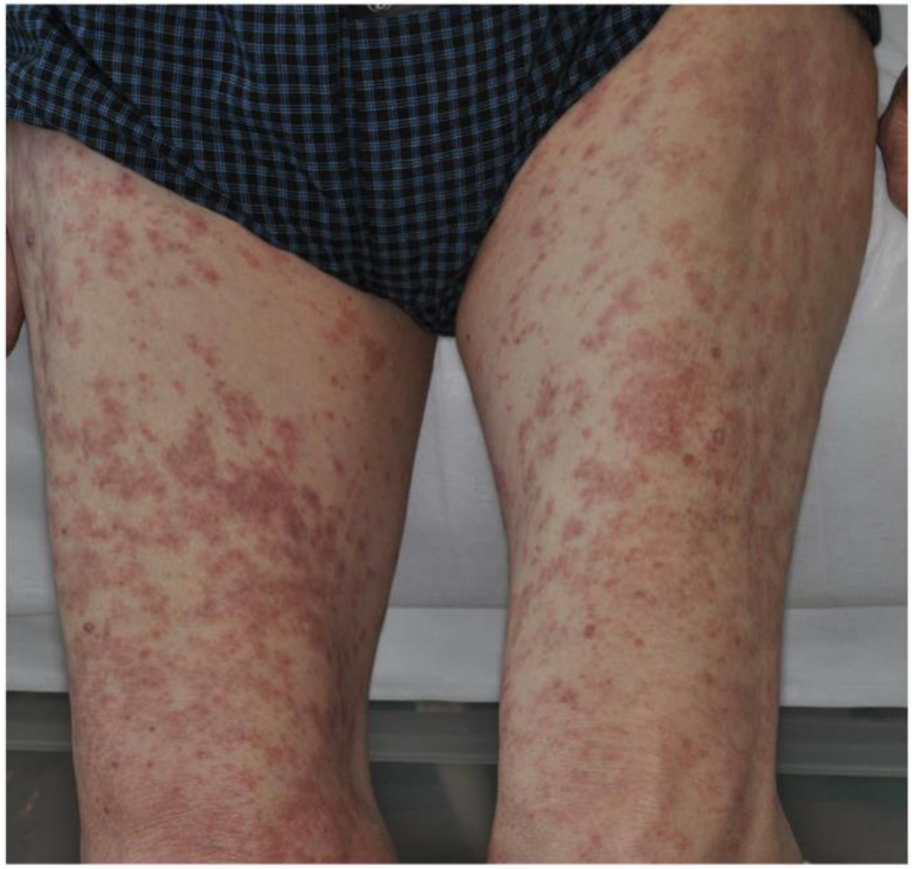
1. **Phenytoin**
2. **CBZ/OxC**
3. **Clonazepam**

What to do if the patient presents with ataxia

- **Check drug levels if possible**
- **Look for other causes of ataxia**
- **Remove the offending drug and replace with another with a favorable adverse effect profile**

A patient with epilepsy presents with this skin finding. Which of the ASMs could be responsible?

1. Carbamazepine
2. Phenytoin
3. Lamotrigine
4. All of the above



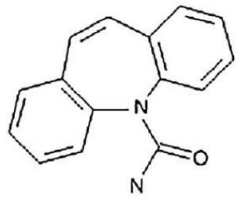
EPILEPSY CURRENTS

Current Literature
In Clinical Science

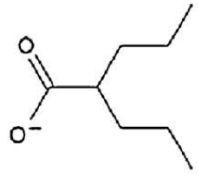
Epilepsy Currents
2019, Vol. 19(2) 96-98

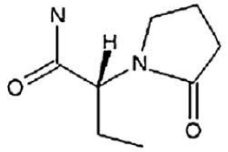
DOI: 10.1177/1535759719835672
journals.sagepub.com/home/epi
SAGE

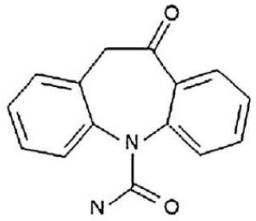
Making Rash Decisions in Epilepsy: Evaluating Hypersensitivity Reactions to Anti-seizure Medications

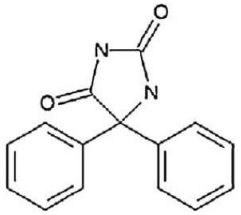

Carbamazepine

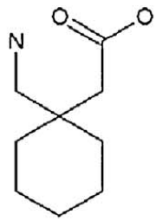

Lamotrigine

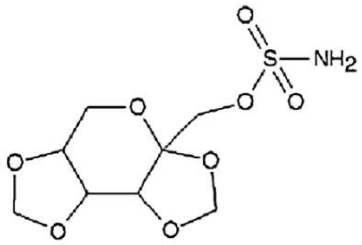

Valproate

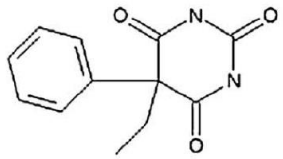

Levetiracetam


Oxcarbazepine


Phenytoin


Gabapentin


Topiramate


Phenobarbital

Non-aromatic structures – lesser risk for cutaneous ADRs

Aromatic structures – high risk for cutaneous ADRs

Always explicitly state risk of rash to the patient

Document in prescription that patient has been explained about the side effect profile

Start low and go slow

Advise patient to review immediately in case of any ADRs

Seek dermatologist confirmation

Don’t re-challenge with same drug or drugs with similar chemical structure

5-year-old child with epilepsy has been brought with hyperactivity and anger outbursts.

Which drug will you avoid in this patient?

- Levetiracetam
- Carbamazepine
- Lacosamide
- Valproate

Drugs to avoid when a child has behavioral issues and cognitive abnormalities

a. **Levetiracetam**
b. **Brivaracetam**
c. **Perampanel**
d. **Topiramate**
e. **Clobazam**

Drugs to avoid when a child has behavioral issues and cognitive abnormalities

a. **Valproate**
b. **Carbamazepine/OxC**
c. **Zonisamide**
d. **Lacosamide**

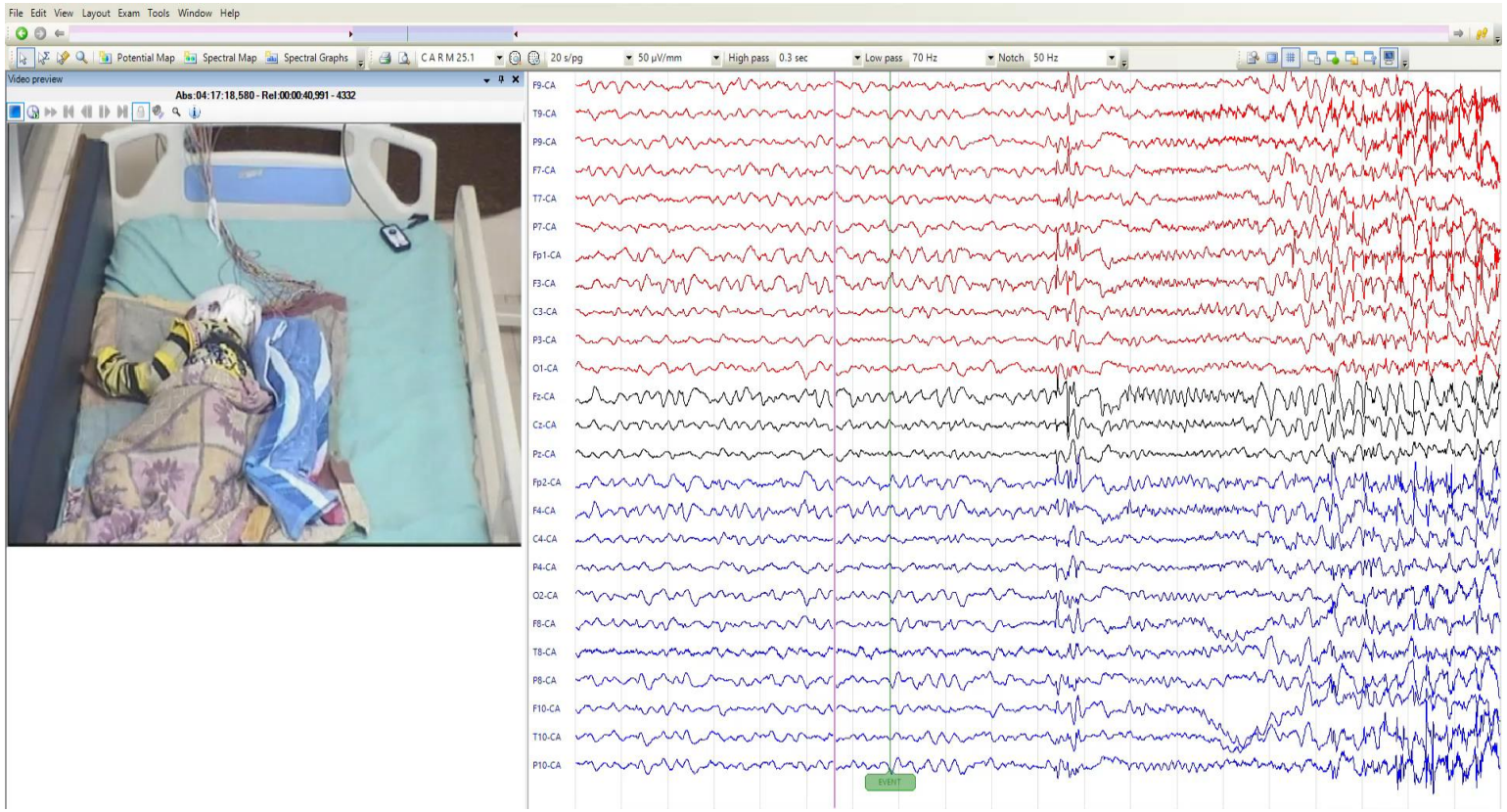
Summary of advantages of various AEDs

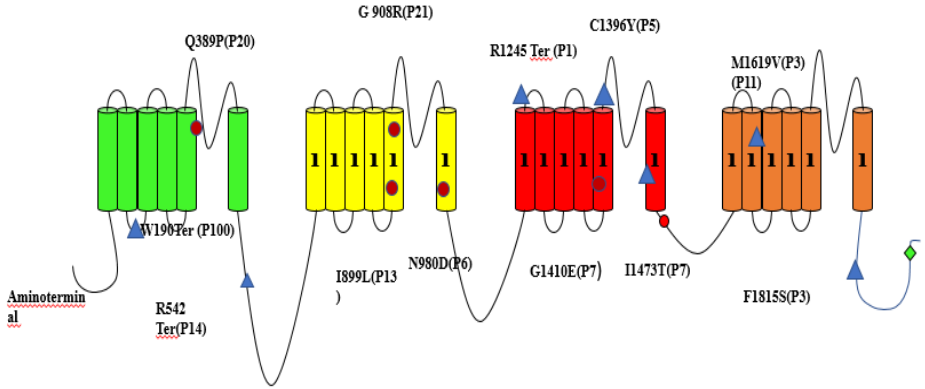
No cognitive effects	No weight gain	Linear kinetics	Minimal protein binding	Rapid titration	No/minimal neuropsychiatric symptoms
OXC LTG LEV VPA,CBZ(minimum)	PHT OXC LTG	OXC LTG LEV	LEV TOP GABAPENTIN PREGABALIN	LEV PREGABALIN GABAPENTIN	LTG VPA ZON

2-year-old with febrile seizures since 6 months of age. From 1.5 years seizures have become frequent and refractory (hemiclonic) with regression of milestones

What drug will you treat this child with?

- Valproate
- Carbamazepine





This patient had a nonsense mutation in SCN1A

VideoEEG : hemiclonic seizure

Underlying epileptic activity hampers development in epileptic encephalopathy – refer these children early!

Dravet Syndrome (DS)

Mutations in SCN1A are present in more than 80% of patients with Dravet syndrome and some families with genetic epilepsy with febrile seizures plus (GEFS)

Mutations in GEFS+ are typically inherited in an autosomal dominant fashion whereas in most patients with Dravet syndrome the SCN1A mutations occur de novo

The SCN1A mutations lead to a loss-of-function of the protein which results in reduced activity of inhibitory neurons

SCN1A related epilepsy

✗

Sodium Channel Blockers

- Carbamazepine
- Lamotrigine
- Phenytoin

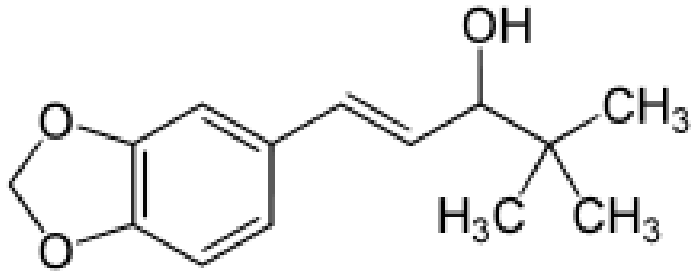
✓

Useful drugs

- Valproate
- Clobazam

Novel Drug

- Stiripentol



Case scenario - Challenge

- 26 year old female, daily wage laborer
- **fever:** started 1 week prior to admission, mild to moderate grade, subsided with over the counter medication in 3 days.
- **Seizures**- 3 days: focal motor either left or right with bilateral tonic clonic movements
- No of attacks before presentation: cluster episodes - 2, day of admission: 3 episodes without regaining sensorium (SE for 3 hours
- No history of other neurological or systemic symptoms
- Not on any medication
- No h/o encephalitic illness, head injury, subnormal intelligence, family history of seizures
- No lateralizing signs

SE: an approach

Buccal/nasal midazolam or rectal diazepam ← Pre-hospital management

iv Lorazepam (0.1 mg/kg) ← Impending SE

iv Phenytoin (20 mg/kg)
or
iv fosphenytoin (15-20 mg/kg)

iv Valproate (30-40 mg/kg)

iv Levetiracetam (30 -40 mg/kg)

Lacosamide? ← Established SE

Early Refractory SE

ICU, Anesthetics etc ← Refractory & Super-refractory SE

iv BZD f/b others ← NCSE

Special Situations and SE

- Pregnancy: Eclampsia - MgSO4
- Elderly: Avoid Phenytoin
- Liver: Levetiracetam/Lacosamide
- Neonates: Phenobarbitone
- Children: BZD followed by Fosphenytoin, phenobarbitone, levetiracetam
- HIV: Levetiracetam, Lacosamide

30-year-old with epilepsy for 10 years. Has 2-3 seizures every month (focal with impaired awareness) and is uncontrolled on 3 ASMs. His MRI shows right mesial temporal sclerosis. What is the next step in the management?

1. Add 4th drug
2. Refer to tertiary center for surgery

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A RANDOMIZED, CONTROLLED TRIAL OF SURGERY FOR TEMPORAL-LOBE EPILEPSY

SAMUEL WIEBE, M.D., WARREN T. BLUME, M.D., JOHN P. GIRVIN, M.D., PH.D., AND MICHAEL ELIASZIW, PH.D., FOR THE EFFECTIVENESS AND EFFICIENCY OF SURGERY FOR TEMPORAL LOBE EPILEPSY STUDY GROUP*

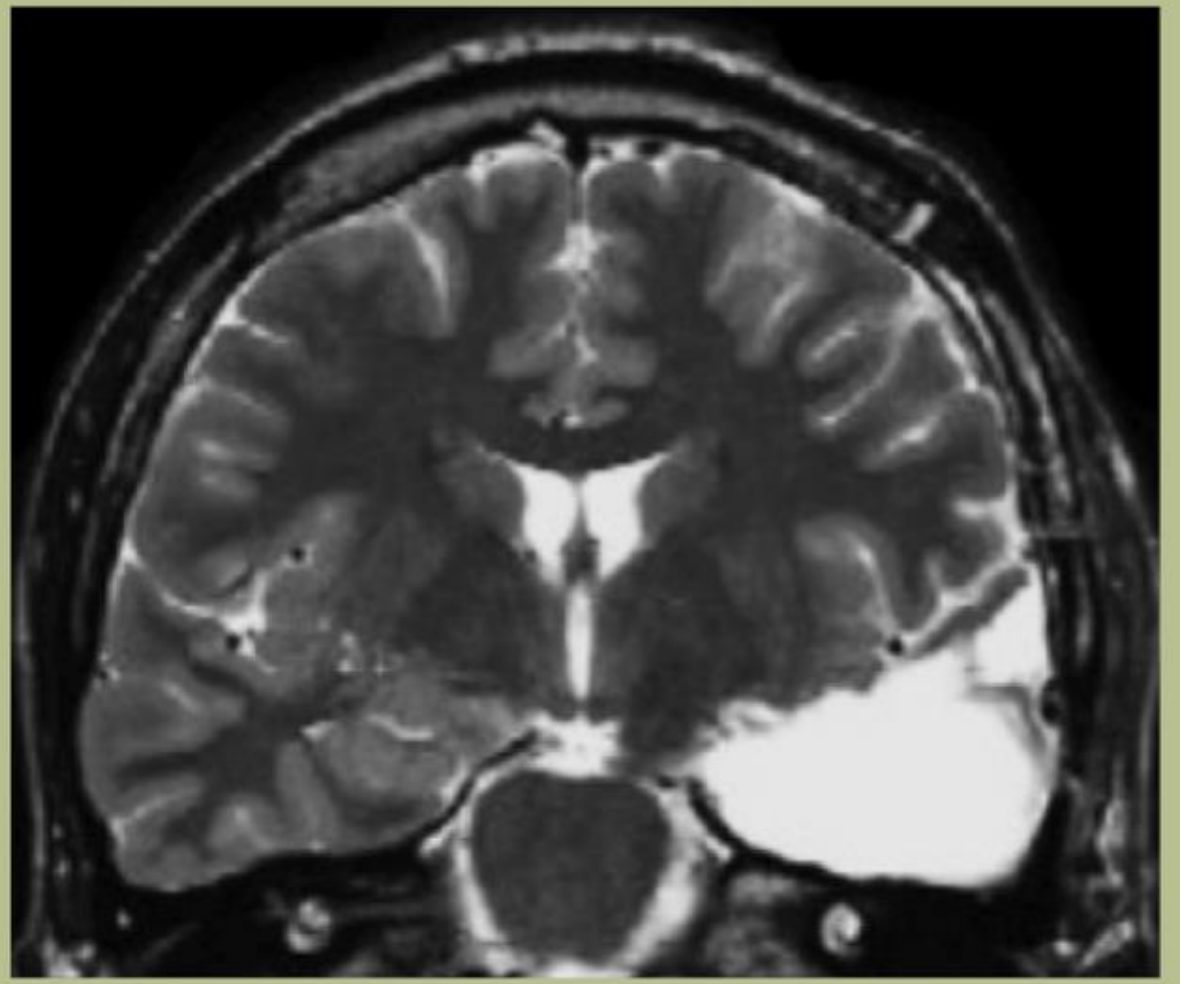
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

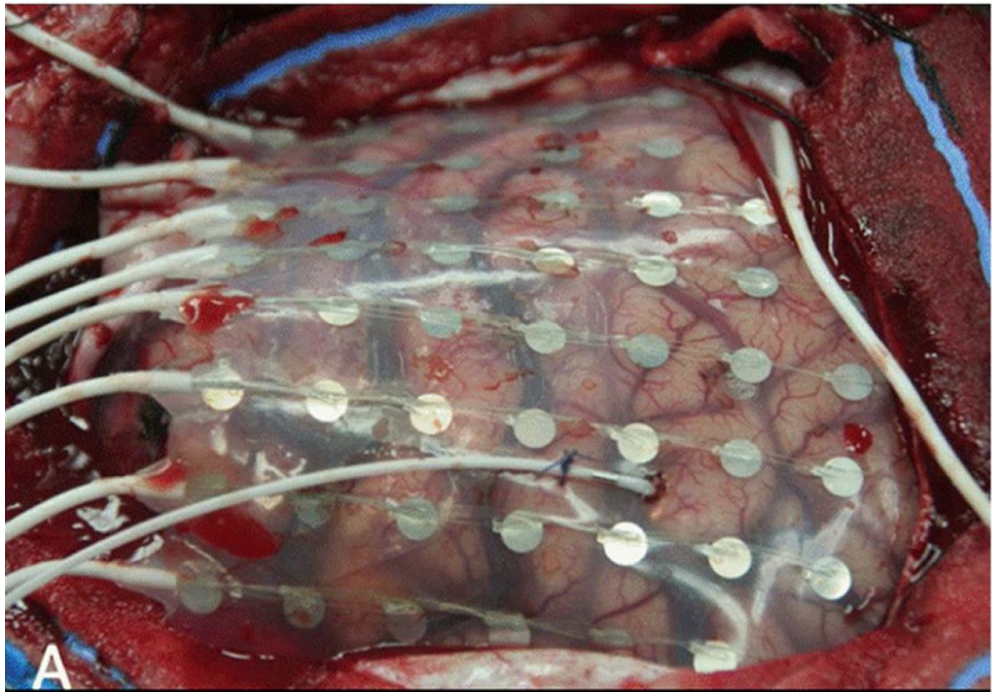
Surgery for Drug-Resistant Epilepsy in Children

Rekha Dwivedi, Ph.D., Bhargavi Ramanujam, M.D., D.M., P. Sarat Chandra, M.Ch., Savita Sapra, Ph.D., Sheffali Gulati, M.D., D.M., Mani Kalaivani, Ph.D., Ajay Garg, M.D., Chandra S. Bal, M.D., Madhavi Tripathi, M.D., Sada N. Dwivedi, Ph.D., Rajesh Sagar, M.D., Chitra Sarkar, M.D., and Manjari Tripathi, M.D., D.M.

- **There is Class I evidence that advocates epilepsy surgery for patients with drug refractory epilepsy**
- **Drug refractory epilepsy – when a patient has failed to achieve sustained seizure freedom with at least two appropriate and well tolerated anti-seizure medications**



- MRI post surgery (anterior temporal lobectomy with amygdalohippocampectomy – ATL+AH)
- Patient is seizure free!



For complex cases, invasive EEG methods may be required

Epilepsy surgery is regularly carried out at NIMHANS (around 1-3/week)

Early referrals lead to better outcomes – if you suspect drug resistant epilepsy, please refer

Review video and opine

Q. What is the next step in management

a. **MRI/EEG and start ASM (Levetiracetam)**
b. **Refer to psychiatry**

12 year old girl, age at onset of epilepsy – 5 years. Seizure free from the last 5 years on a single drug (carbamazepine).

Q1. Do you think drugs can be tapered in epilepsy

- Yes
- No

Q2. Is the risk of recurrence on tapering same for children and adults?

- Yes
- No

Treatment Challenge:

- Patient wants to know if she is “cured”?
- And, can she then stop her anti-seizure medications?

When we call “Epilepsy resolved?”

- Previous inadequacies are as follows:
  - Traditional definition does not allow for epilepsy to disappearance.

    a. seizure free from Childhood absence

    b. epilepsy patients with MTLE who have been seizure-free off medications for 10 years after resection of their hippocampal sclerosis

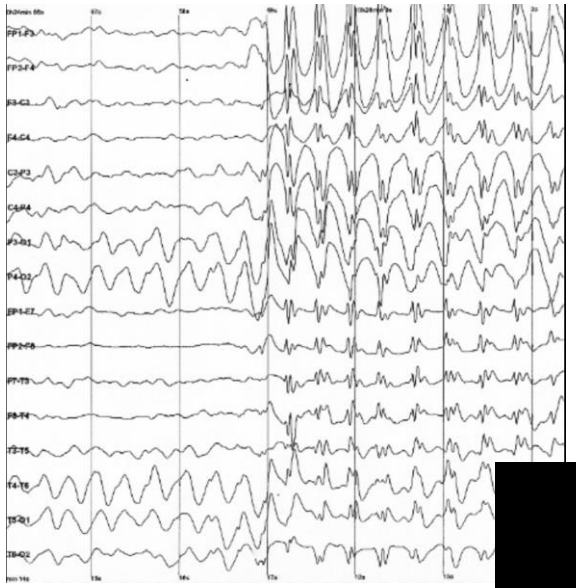
    c. Children outgrowing BECTS
- Task Force definition:
  - Epilepsy is resolved for individuals:
    - who had an age-dependent epilepsy syndrome and are now past the applicable age
    - those who have remained **seizure-free for the last 10 years, with no seizure medicines for the last 5 years.**

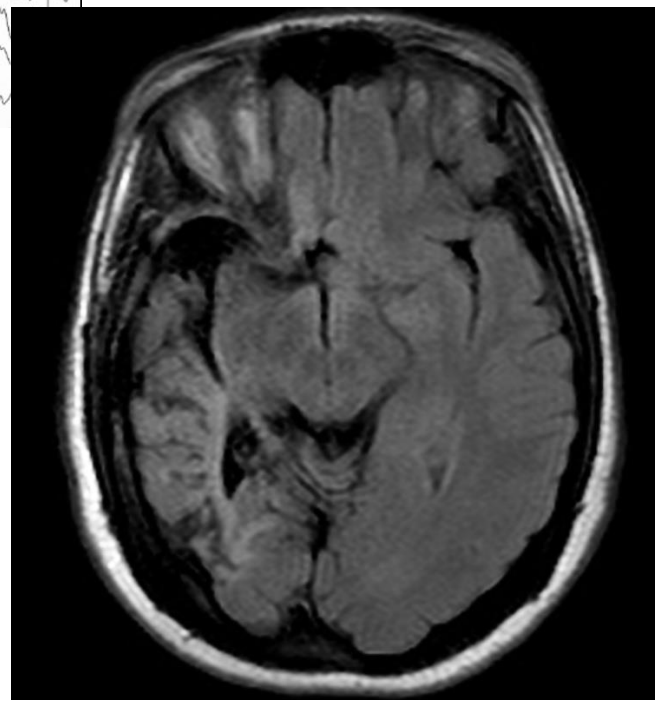
Points remember while tapering drugs

- **Drugs available are ANTI-SEIZURE medications and not truly ANTI-EPILEPTICS. They do NOT modify the underlying disease process**
- **Some epilepsies are age limited (e.g. CAE, CECTS) – underscores importance of identifying etiology. After a particular age the epileptogenic process may remit**
- **On the other hand some epilepsies are “lifelong” – e.g. JME – drug taper is very risky**
- **Children have lesser recurrence rate compared to adults after drug tapering (~30% vs ~40%)**

Risk factors associated with seizure recurrence

- **The epilepsy syndrome (eg JME) and symptomatic epilepsies**
- **Took a long time (many years) to achieve seizure freedom**
- **Abnormal neurological examination**
- **EEG prior to planning drug taper or during drug taper shows ongoing IEDs**
- **Associated intellectual subnormality**





When and how to stop?

- **Controversial and debated topic**
- **Time to taper – varying recommendations available (2-3years for children and 4-5 years for adults)**
- **Slow vs. rapid taper – there is no clear difference between the two methods in literature but from personal experience, we recommend a slow taper (over 3 months)**

Take home message

- **The management of epilepsy pivots on the etiology suspected**
- **Acute symptomatic epilepsies do not need long term medications**
- **Always re-check compliance when a patient has a “breakthrough” seizure**
- **Monitor for adverse effects while on ASMs, especially in special populations**
- **Diagnose refractory epilepsies early and refer**

Thank you

Questions??