



ASMs: Selection, Initiation and Discontinuation

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30/11/68

30 Nov 2025

Epilepsy Course for Neurology Residents and Pediatric Neurology Fellows

30/11/68

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สมาคมโรคลมชักแห่งประเทศไทย
Epilepsy Society of Thailand

ครั้งที่
16

Epilepsy Course for Neurology and Pediatric Neurology Residents

วันที่ 29-30 พ.ย. 68 ณ โรงแรม บางแสน เซอร์วิทจ จ.ชลบุรี

SATURDAY 29 NOVEMBER 2025

08:30 - 08:45 Opening remark รศ.พญ.นภวรรณ บุญญพิสิฏฐ์ Moderator: รศ.พ.ว.ฉันท คณดิสรรม 08:45 - 09:45 Workshop - Epileptic seizure vs seizure mimickers - Seizure semiology พ.อ.หญิง รศ.กิริติ สุวรรณศักดิ์ อ.พ.พัชรินทร์ ตรีสุทธาธิ์ 09:45 - 10:30 Wrap-up 10:30 - 10:45 Break Moderator: ผศ.พญ.กมลวรรณ กติญญวงค์ 10:45 - 11:15 Natural history of epilepsy ผศ.พ.ว.รพีพัฒน์ เทวมิตร 11:15 - 11:45 SUDEP รศ.พ.ว.อริวัฒน์ สุนทรพันธ์ 11:45 - 12:45 Lunch	Moderator: อ.พญ.สุดา จิรสกุลเดช 12:45 - 13:45 Workshop - Epilepsy syndromes in neonates/infants/children - Epilepsy syndromes of adolescence/adulthood ผศ. (พิเศษ) นพ.กุลสฤทธ ศักดิ์พิชัยสกุล อ.พญ.สุดา จิรสกุลเดช อ.พญ.ชานนดี สมบุญรัตน์ 13:45 - 14:30 Wrap-up 14:30 - 14:45 Break 14:45 - 15:15 Neuroimaging in epilepsy อ.พญ.ปัญจมา เลิศบุษยาบุตุล 15:15 - 15:45 Genetic testing in epilepsy ผศ.นพ.มงคล ชานวณิชตระกูล 15:45 - 16:15 Psychiatric comorbidities in epilepsy อ.พญ.ญานิน ทิพากร เกียรติปานอกกุล 16:15 - 16:30 Q & A
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SUNDAY 30 NOVEMBER 2025

Moderator: รศ.พ.ว.อริวัฒน์ สุนทรพันธ์ 08:00 - 08:45 Pharmacology in epilepsy รศ.ดร.กช.ธนรัตน์ สรอสณห์ 08:45 - 09:15 ASMs selection, initiation, and discontinuation ผศ.พญ.กมลวรรณ กติญญวงค์ 09:15 - 09:45 Selection of ASMs in special population รศ.พญ.นภวรรณ บุญญพิสิฏฐ์ 09:45 - 10:00 Q & A 10:00 - 10:15 Break	Moderator: พ.อ.พญ.พาสี สิกรินามสุวรรณ 10:15 - 10:45 Management of drug resistant epilepsy อ.พ.ศ.ธีรารุณ วงษ์เย็นจันทร์ 10:45 - 11:15 Presurgical evaluation and epilepsy surgery อ.พ.ศ.สุกสิณี เขียวรัตน์พันธ์ 11:15 - 11:45 Status epilepticus พ.อ.พญ.พาสี สิกรินามสุวรรณ 11:45 - 12:00 Q & A 12:00 - 13:00 Lunch
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ขอเชิญเฉพาะแพทย์ประจำบ้านสาขาสารภวิทยา ปีที่ 3 แพทย์อนุสาขาสารภวิทยาโรคลมชัก ปีที่ 1, 2 และแพทย์ประจำบ้านต่อยอด สาขากุมารเวชศาสตร์สาขาสารภวิทยา ปีที่ 2 เข้าร่วมการอบรมครั้งนี้ (โดยไม่มีค่าใช้จ่าย)

Outline

- *ASM Selection (from previous lecture)*
- ASM Initiation
- ASM Discontinuation

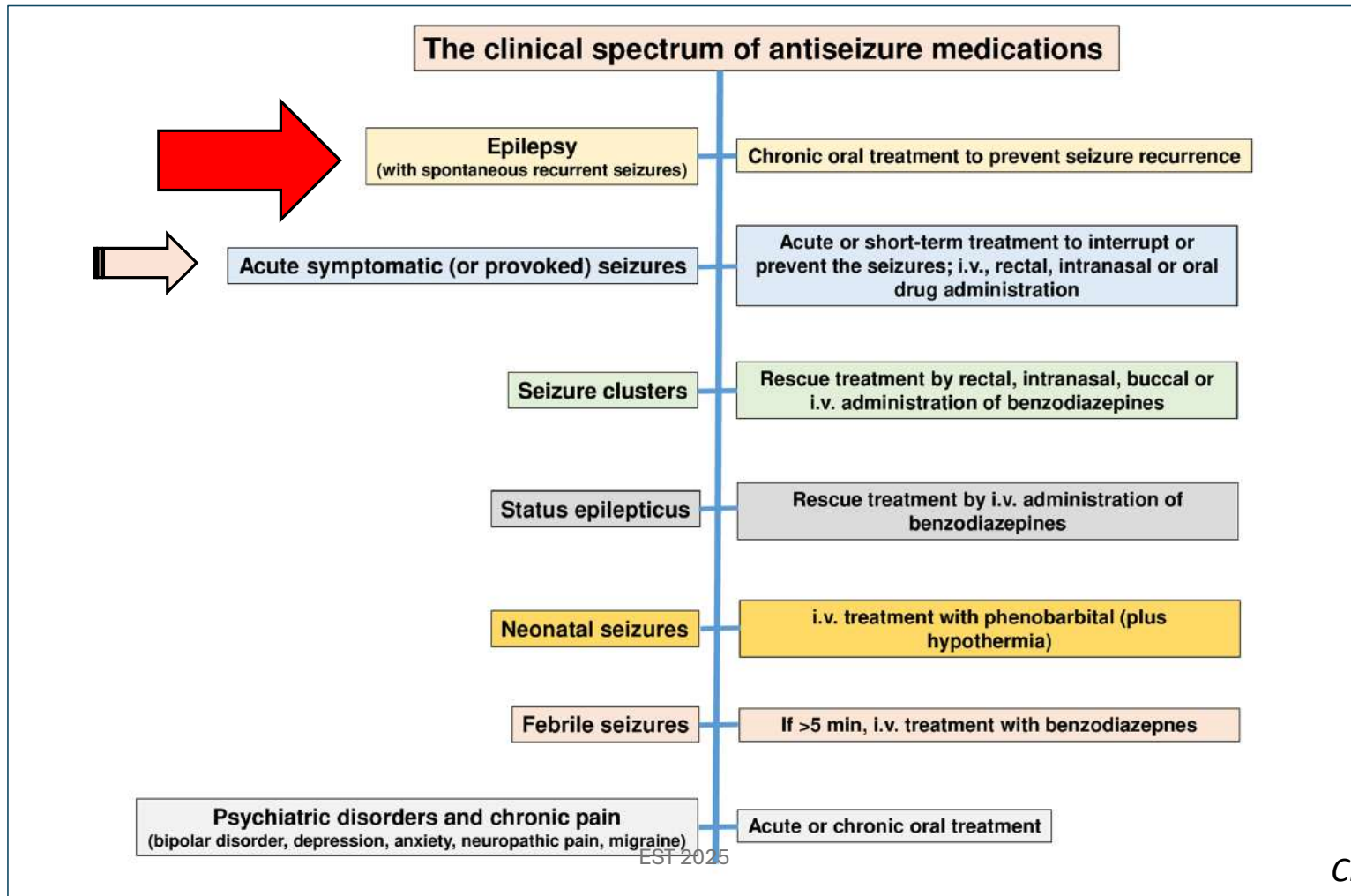
ASMs Selection

Core principles

1. Seizure type and epilepsy syndrome
2. Age-specific consideration: Pediatric vs Adult
3. Comorbidities and drug interactions

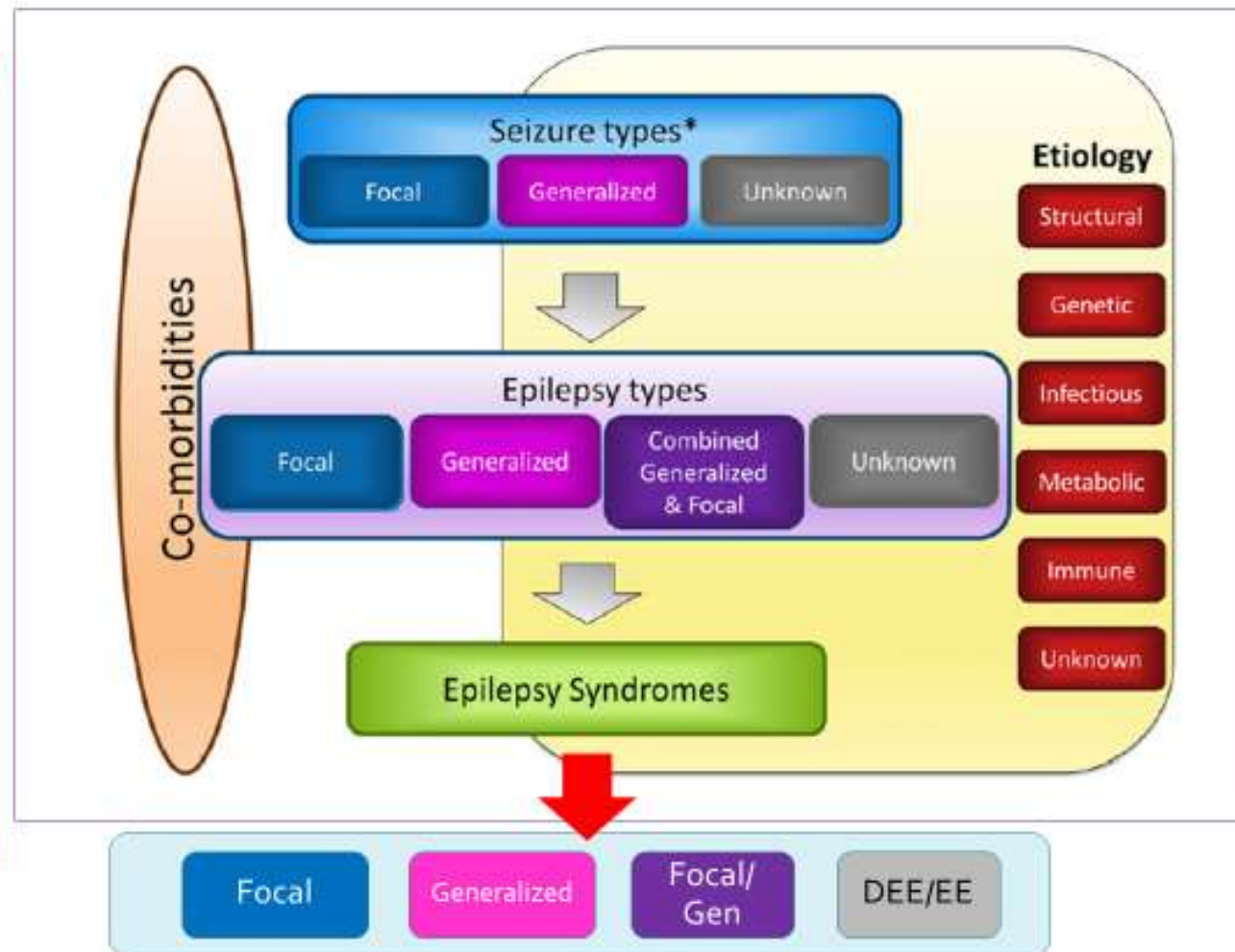
Issue of interest: Classic vs Newer ASMs

The Clinical Spectrum of ASMs



Epilepsy Classification 2017

+ Epilepsy syndromes 2022



Variables that affect a specific ASMs

ASM specific variables	Patient-specific variables	Nation-specific variables
• <u>Sz type or syndrome efficacy/effectiveness</u> • Pharmacokinetics • Interaction potential • Formulation • Dose-dependent ADR • Idiosyncratic reaction • Chronic toxicity • Teratogenicity • MOA • Rational Rx (mono vs polyRx)	• <u>Age, Gender</u> • Genetic BG • <u>Comorbidities</u> • Co-medications • Ability to swallow tablets • Insurance coverage • Relative wealth • <u>Sz type and syndrome</u> • <u>Stage of the epileptic condition</u>	• AED availability • AED cost • ปัญหาค่ายาและการเบิกจ่าย

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Adapted from *Epilepsia* 47,2006

ASM Selections @ Seizure Type/Syndrome

1. 1.1 First seizure (acute symptomatic sz **or** unprovoked sz) [Hx, PE, Ix]
1.2 Epileptic syndrome [Hx, EEG]
2. Whether it is a first one or the patient does not remember?
3. Does the patient need to start Rx after first seizure?
4. ***Epilepsy** (2 unprovoked sz/ 2 reflex sz)*



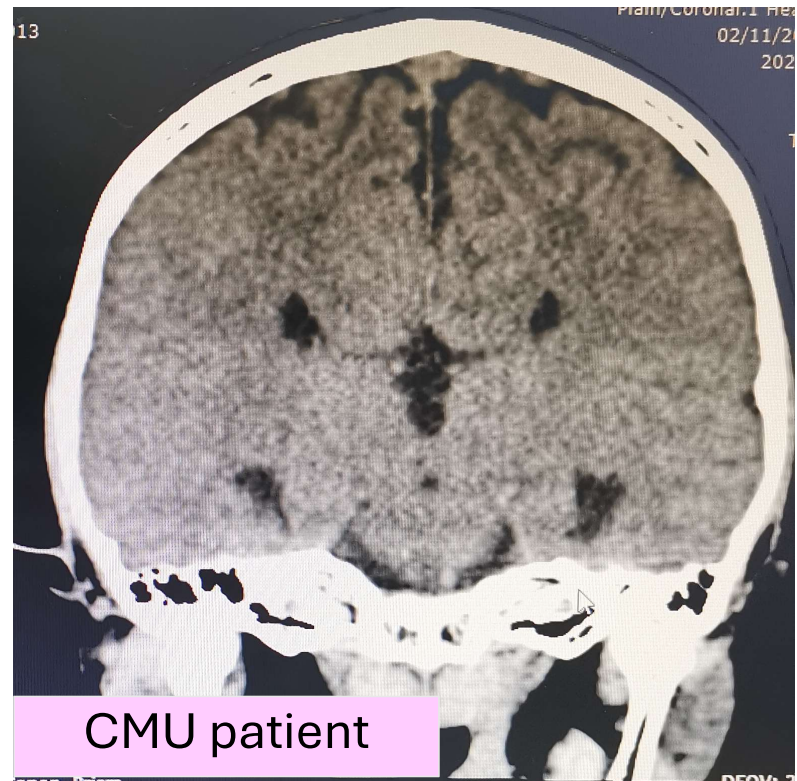
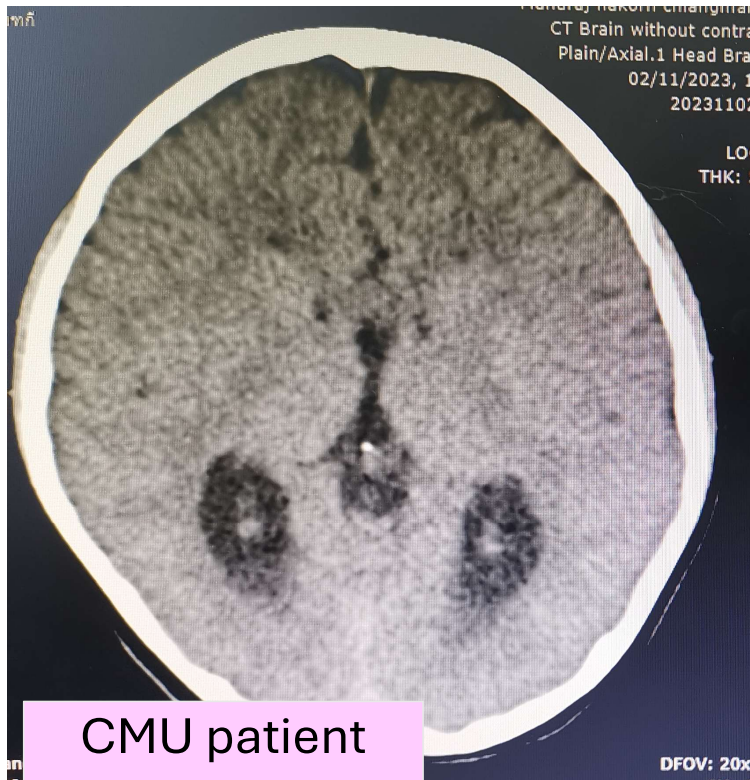
First seizure

Real-life Scenario

Case Scenario-1

- ดญ ไทย อายุ 10 ปี ระหว่าง**ยื่นเข้าแถว**ที่โรงเรียน ครูสังเกตเห็น วูบล้มหงายหลัง มีอาการเกร็งแขนขา ตาลอยปากเขียว หน้าซีด 45-60 วินาที
- ไม่มีประวัติสภาวะ อูจระวาด
- **สะดุ้งสะดือนาน 10** นาที หลังจากนั้นถามตอบรู้เรื่อง แต่จำเหตุการณ์ไม่ได้ ร.ร. แจ้งญาติ จากนั้น นำส่ง รพ
- ที่ ER มีอาการ 2 ครั้ง แต่ภายหลังรู้ตัวดี และตรวจร่างกาย**ไม่มี focal deficit**
- Basic lab = normal
- Other Ix: need CT brain ?
- Diagnosis = ?
- Treatment issue: need ASMs?

CT brain



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First episode unprovoked seizure

Case Scenario-2

- เด็กชาย อายุ **10** ปี มีอาการปวดศีรษะตอนกลางคืน ตอนเช้าแม่ไปเรียก ดูสะลึมสะลือมาก และมีแขนข้างซ้ายอ่อนแรง ช่วงสายมี**อาการเกร็ง กระตุก 1** นาทีบนเตียง
- นำส่ง ER ไม่มีอาการชัก แต่ **clinical obtundation**
- Imaging as picture
- Diagnosis = ?
- What would you do in this case?

Acute symptomatic seizure (from stroke)

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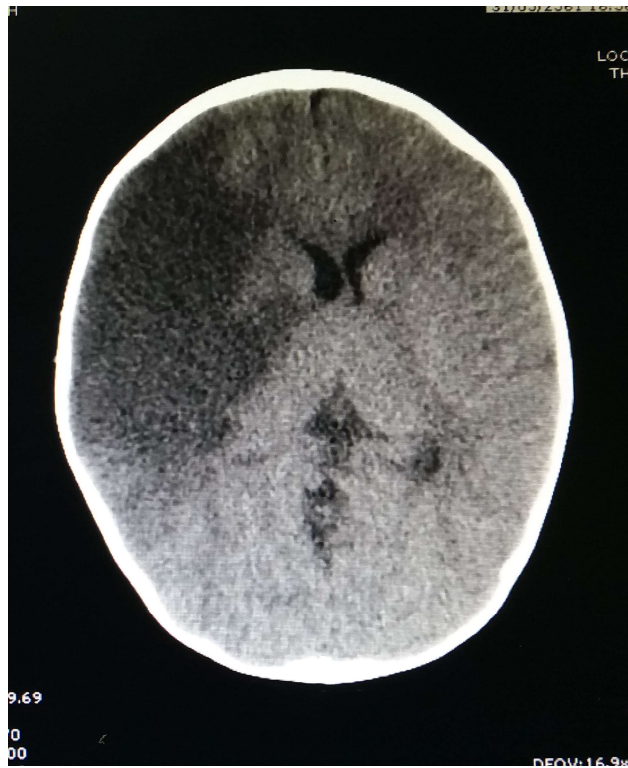
CMU patient

[Hx, PE, Ix]

	Acute symptomatic sz	
Stroke	33%	

CT brain

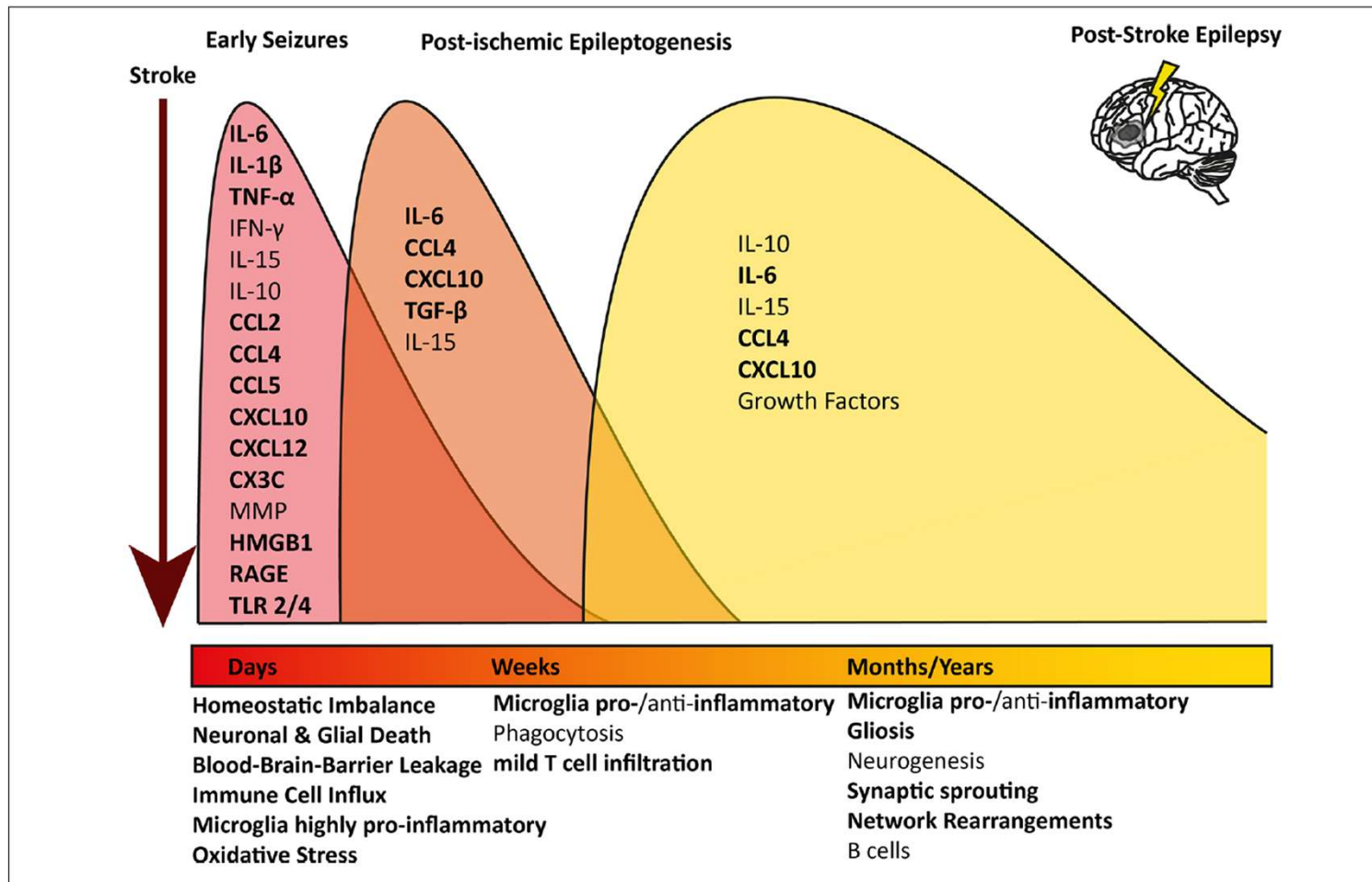
CMU patient



CT during acute symptomatic seizure

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	Acute symptomatic sz	Unprovoked seizure
Stroke		71%

CT brain

CMU patient



CT during acute symptomatic seizure

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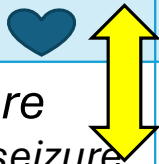


CT 4 weeks later

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Definition and Terminology

Epilepsy <i>ILAE 2014</i>	- At least two unprovoked (2 reflexes) seizures more than 24 h apart or one unprovoked seizure with a probability of a subsequent seizure <u>recurrence risk</u> of approximately 60% (similar to 10-year recurrence risk after two unprovoked seizures) or - Diagnosis of epilepsy syndrome
Acute symptomatic seizure	Caused by acute illness (stroke, CNS infection, TBI): seizure within 7 days of an insult
<i>Provoked seizure</i> <i>Situation-related seizure</i>	Caused by transient reversible alterations without structural change (toxin, metabolic factors, medication); occurs at time of insult or within 7 days
Unprovoked seizure	Seizure occurring in the absence of a potentially responsible clinical condition or beyond the interval estimated for the occurrence of acute symptomatic seizures
Remote symp' seizure (unprovoked seizure)	Pre-existing brain injury: seizure greater than 7 days after insult



Patient: children or adults

First seizure:

[Hx, PE, Ix]

1st Acute Symptomatic Seizure

(structural or non-structural)

VS.

1st Unprovoked Seizure

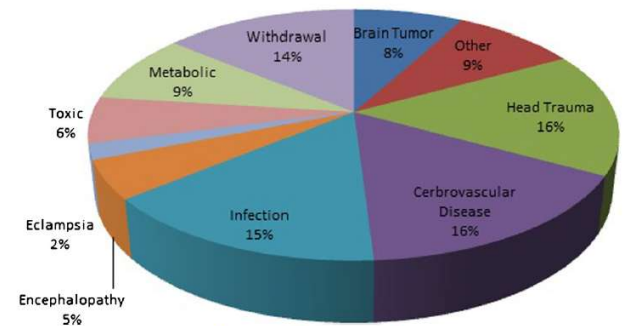


Fig. 1. Etiologies of acute symptomatic seizures [2] (copyright 2005 by ILAE. Adapted with permission).

Acute Symptomatic

First Unprovoked

Cumulative Risk in 2 Important Issues

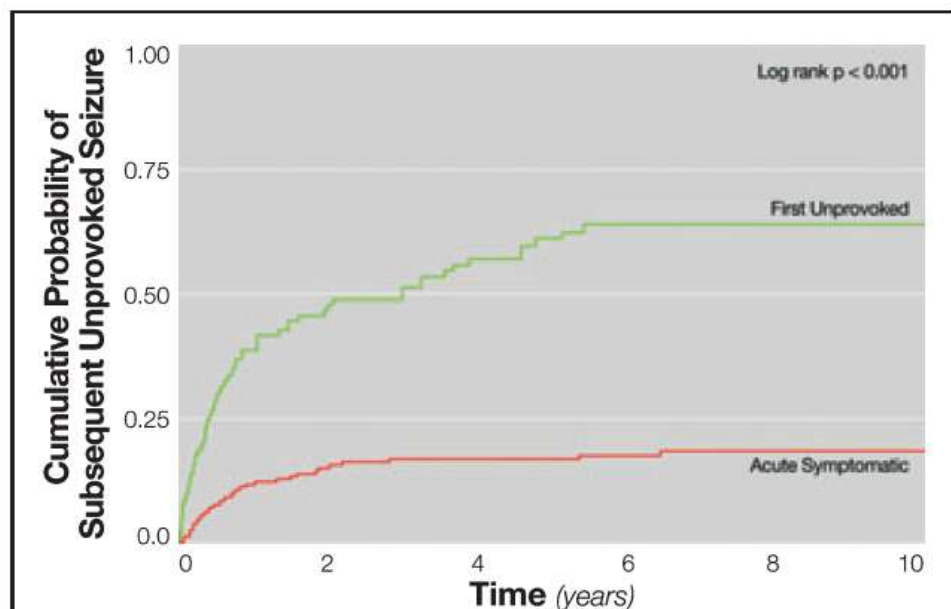


Figure 3.

Cumulative risk of subsequent unprovoked seizure after first acute symptomatic seizure and first unprovoked seizure.

Epilepsia © ILAE

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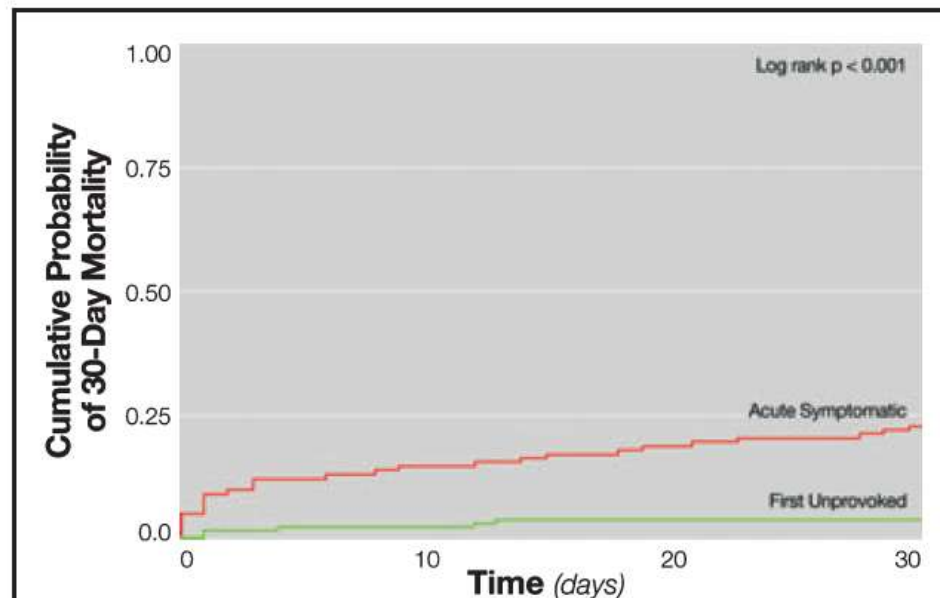


Figure 1.

Cumulative risk of death in the first 30 days after first acute symptomatic seizure and first unprovoked seizure.

Epilepsia © ILAE

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Epilepsia, 50(5):1102–1108, 2009



ASM Initiation



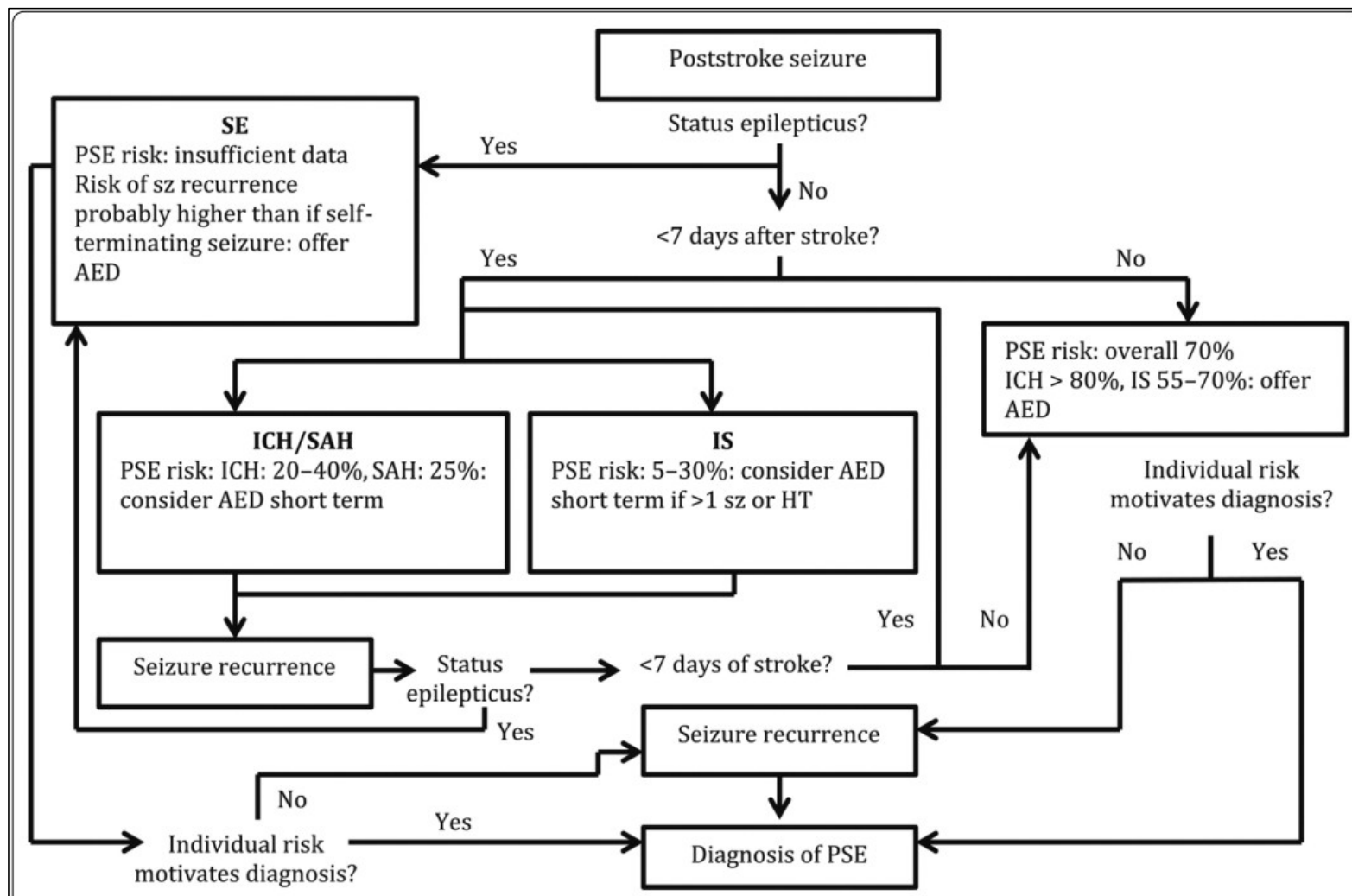
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Management Guideline in Acute Symptomatic Seizure

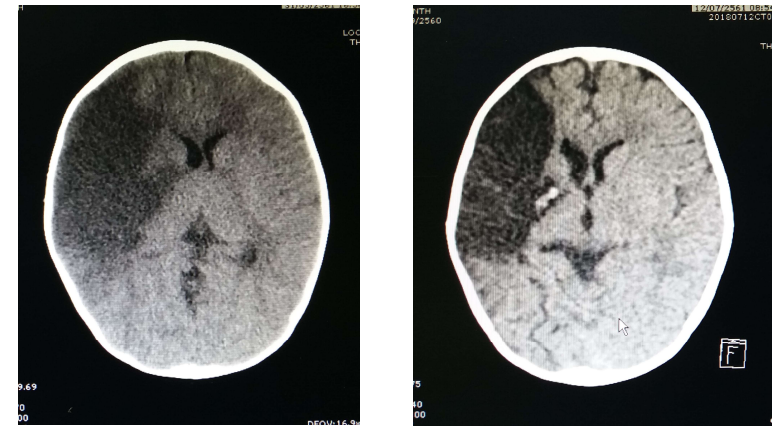
Etiology of sz	Type of sz	Short-term ASM	Long-term ASM
Ischemic, Hge, subdural, SAH	Acute symptomatic	a short course may be necessary due to higher mortality rates in the short term	if pt develops remote symp sz in setting of underlying lesion
CVST	Acute symptomatic	- up to 6 mo–1 yr of ASM Rx may be necessary due to higher mortality rate in the short term and ↑risk of unprovoked sz with : hemorrhagic infarcts, : sup^r sagittal thrombosis, : Hx of acute symp seizures	if pt develops remote symp sz in setting of underlying lesion



Important risk factors of **PSE**

CMU's
patient

- Stroke severity
- Cortical location
- Young age at stroke
- Hemorrhage
- Total anterior circulation infarction



Management Guideline in Acute Symptomatic Seizure

Etiology of sz	Type of sz	Short-term ASM	Long-term ASM
Trauma	Acute symptomatic	• 1 week of ASM • Longer (1–3 mo of Rx) in mod-severe depressed skull fx, penetrating injury, subdural requiring evacuation, multiple contusions, epileptiform EEG, prolonged period of LOC or amnesia	• if pt develops remote symp sz in setting of underlying lesion

Management Guideline in Acute Symptomatic Seizure

Etiology of sz	Type of sz	Short-term ASM	Long-term ASM
CNS infection	Acute symptomatic	- A short course is necessary due to high mortality in short term - Consider 1–3 mo of Rx in pts with viral encephalitis	if pt has remote symp sz or unprovoked sz with structural lesion

First Unprovoked Seizure

Initial Rx of 1st Unprovoked Seizure

- **Reduce** recurrent risk of 2nd unprovoked seizure
- **No** difference in likelihood of long-term epilepsy remission

Table 2 Rates for short-term (1 and 2 years) seizure recurrence after an unprovoked first seizure in adults as related to immediate antiepileptic drug treatment (Class I and II studies)

Ref.	Class	No.	Treated, n (%)	Recur. rate treated, n (%)	Recur. rate untreated, n (%)	Length of follow-up, y
12-14	I	397	204 (51)	36 (18) ^a	75 (39)	2
18	II	76	36 (47)	4 (11) ^a	18 (45)	1
15	II	812	404 (50)	129 (32)	159 (39)	2
21	II	228	113 (50)	5 (4) ^a	63 (55)	1
22	II	87	45 (52)	9 (20) ^a	28 (66)	2
Total		1,600	804 (50)	183 (23)	343 (43)	1 or 2

Table 3 Rates of 2-year seizure remission over the longer term (>3 years), comparing immediate with deferred antiepileptic drug treatment of an unprovoked first seizure in adults (Class I and II studies)

Ref.	Class	No.	Immediate treatment, n (%)	Remission, immediate treatment, n (%)	Remission, deferred treatment, n (%)	Length of follow-up
12-14	I	419	215 (51)	174 (81), NS	159 (78)	More than 3 y ^a
15	II	812	404 (50)	372 (92), NS	375 (92)	5 y ^b
Total		1,231	619 (50)	546 (88)	534 (87)	

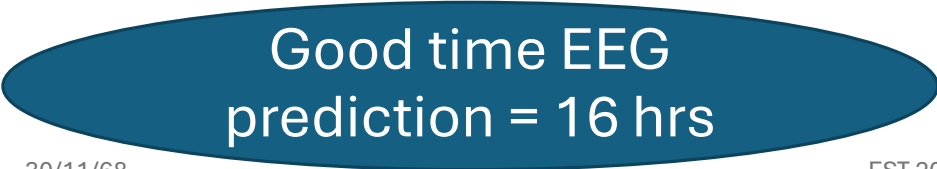
Seizure Recurrence in Children

- After an unprovoked sz: 42% had subsequent seizures
- Cumulative risk at 1 yr = 29% , at 2 yr = 37%, at 3 yr = 42%
- **Risk factors for sz recurrence:** remote symptomatology, abnormal EEG, seizures in sleep, Hx of prior febrile seizures and Todd paralysis
- Risk of seizure recurrence with normal EEG = 30% over 5 yrs
 - with non-specific abn EEG = 45%
 - with epileptiform EEG = 60%



Factors that are indicative for the initiation of ASMs therapy after a first seizure

1. High syndrome-dependent risk of sz relapses (JME)
2. A first seizure with loss of consciousness
3. Adult age
4. Abnormal EEG findings with epileptiform discharges
5. Abnormal MRI finding
6. A high personal risk in case of seizure relapses due to casual habits or professional circumstance



Good time EEG
prediction = 16 hrs

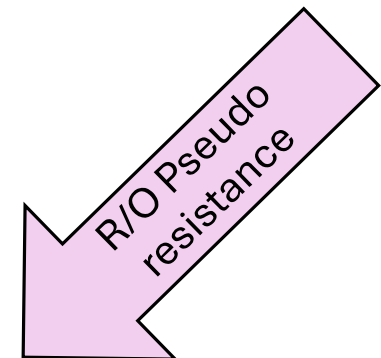
ASM Decision Making

Hx, PE, Ix

- **Initiation:** primary monoRx

: **Broad spectrum ASM** → generalized sz, genetic generalized sz, unknown etiology

: **Narrow spectrum ASM** → focal sz



- **Uncontrolled sz:** 2nd/3rd monoRx **or** polyRx

Broad spectrum vs Narrow spectrum ASMs

VPA
TPM, ZNS
LTG
LEV
PER
RFN
CLB (CLN), CZP
PB
~~PRM, FBM~~

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PHT
CBZ, ~~ESL~~
OXC
VGB
PGB, GBP
LCM
~~TGB~~
~~EZG~~

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Desirable Pk Properties of an ASM

High oral
bioavailability

Low plasma
protein binding

Linear kinetics

Ready
penetration
across the BBB

Long half-life

No active
metabolites

Significant renal
elimination

Elimination, not
involving
oxidation or
conjugation

Low vulnerability
to drug
interactions

Table 1 Spectrum of antiseizure effects of approved antiseizure medications in preclinical seizure models and patients with epilepsy

Drug	Efficacy in preclinical rodent models				Clinical efficacy						
	Primary generalized tonic-clonic seizures (MES test)	Focal seizures (6-Hz test; 32 or 44 mA)	Focal seizures (kindling)	Absence seizures (GAERS or WAG/Rij rat strains)	Focal-onset seizures	Primary generalized seizures			Lennox-Gastaut syndrome	Infantile spasms (West syndrome)	Dravet syndrome
						Tonic-clonic	Absence	Myoclonic			
Acetazolamide ^a	+	?	?+	?	?+	?+	?+	?+	?	?	?
Brivaracetam	+	+	+	+	+	?+	?+	?+	?	?	?
Cannabidiol	+	+	?+	?	+	?	?	?	+	?	+
Carbamazepine	+	?+	+	0	+	+	0	0	0	0	0
Cenobamate	+	+	+	+	+	?	?	?	?	?	?
Clobazam	+	+	+	?	+	+	?	+	+	?+	+
Clonazepam ^a	+	+	+	+	+	+	?	+	?+	?+	?+
Eslicarbazepine acetate	+	+	+	?	+	?	?	?	?	?	?
Ethosuximide	0	0	0	+	0	0	+	0	0	0	?+
Felbamate	+	+	+	?	+	+	?+	?	+	+	?
Fenfluramine	?+	?+	0	?	?	?	?	?	?	?	+
Gabapentin	+	+	+	0	+	?+	0	0	?	?	0
Lacosamide	+	+	+	?	+	+	?	?	?	?	?
Lamotrigine	+	0	+	+	+	+	+	+	+	?+	0
Levetiracetam	0	+	+	+	+	+	?+	+	?+	?	+
Oxcarbazepine	+	?	+	0	+	+	0	0	0	0	0
Perampanel	+	+	+	0	+	+	?+	?+	?+	?	?+
Phenobarbital	+	+	+	+	+	+	+	0	?	?	?+
Phenytoin	+	?+	+	0	+	+	0	0	0	0	0
Pregabalin	+	+	+	0	+	?	?	?	?	?	0
Primidone	+	?	0	0	+	+	0	?	?	?	?
Retigabine (ezogabine) ^b	+	+	+	0	+	?	?	?	?	?	?
Rufinamide	+	+	0	?	+	+	?+	?+	+	?	0
Stiripentol	+	?	?	?	+	+	?+	+	?+	?+	+
Sulthiame ^c	+	?	?	?+	?	?	?	?	?	?+	?
Tiagabine	0	+	+	0	+	?	0	?	?	?+	0
Topiramate	+	0	+	+	+	+	?	+	+	?	+
Valproate	+	+	+	+	+	+	+	+	+	+	+
Vigabatrin	0	?	+	0	+	?+	0	0	?	+	0
Zonisamide	+	+	+	?	+	?+	?+	?+	?+	?+	+

Data sourced from various publications [5, 11, 29, 62, 63, 168, 169] and a PubMed search of recent literature

GAERS genetic absence epilepsy rat from Strasbourg, Hz Herz, MES maximal electroshock seizures, WAG/Rij Wistar Albino Glaxo from Rijswijk, + indicates efficacy, 0 indicates inefficacy or worsening of seizures, ?+ indicates inconsistent or preliminary findings, ? indicates insufficient data

Aggravation of seizure by ASMs

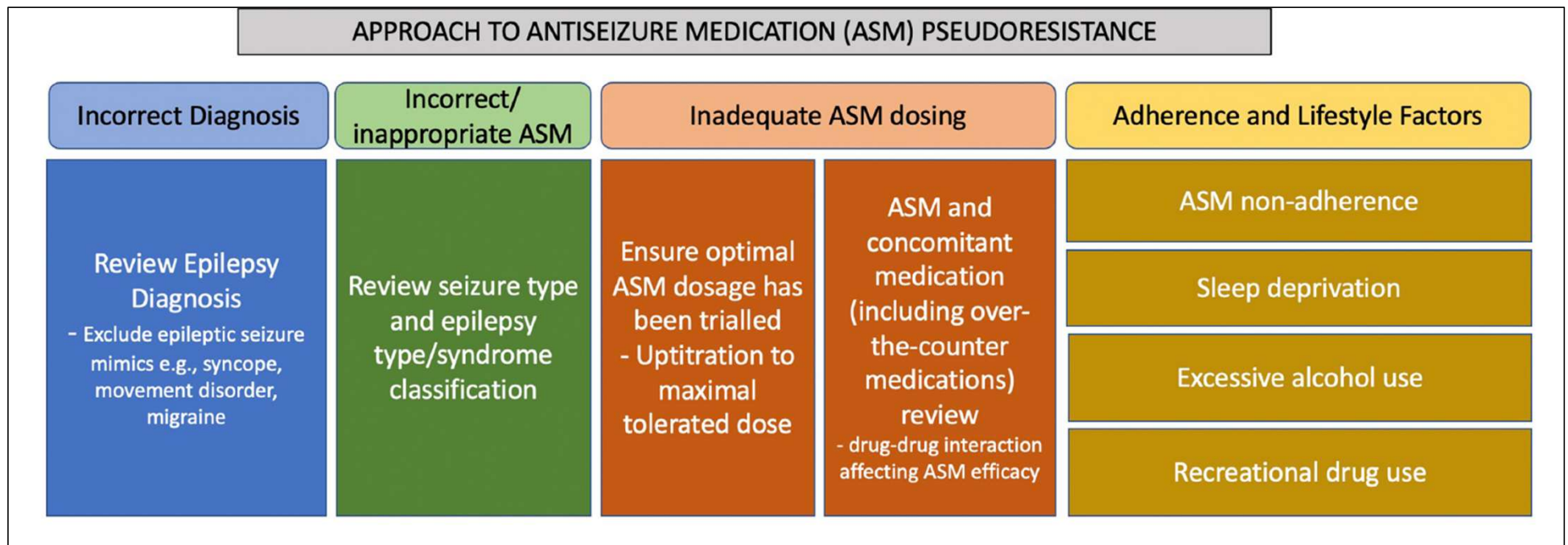
Seizure type/syndrome	Avoid
Myoclonic seizure	PHT, CBZ, OXC, VGB, GBP, PGB, TGB
	<i>Use with precaution: LTG</i>
Absence seizure	PHT, CBZ, OXC, VGB, GBP, PB (high dose), TGB, CLB, CLZ
Tonic seizure (in LGS)	?
CSWS/ESES	?
Dravet syndrome	Sodium channel blockers
LGS	CBZ, OXC, PHT, TGB

Pearls of initiation of ASMs



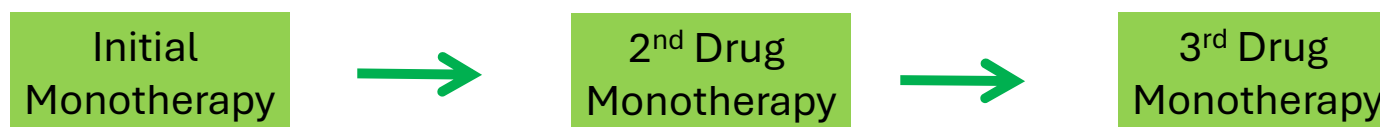
1. Start low, go slow (except when seizures are urgent/severe)
2. Avoid rapid titration of LTG (rash) and TPM (cognitive)
3. Therapeutic drug monitoring when indicated: VPA, CBZ, PHT, PB
4. Check baseline labs
5. Assess response early (4-8 weeks depending on drug titration)
6. Educate caregivers (missed doses, expected SE, warning signs for rash and behavioral change)

When Seizure is Uncontrolled

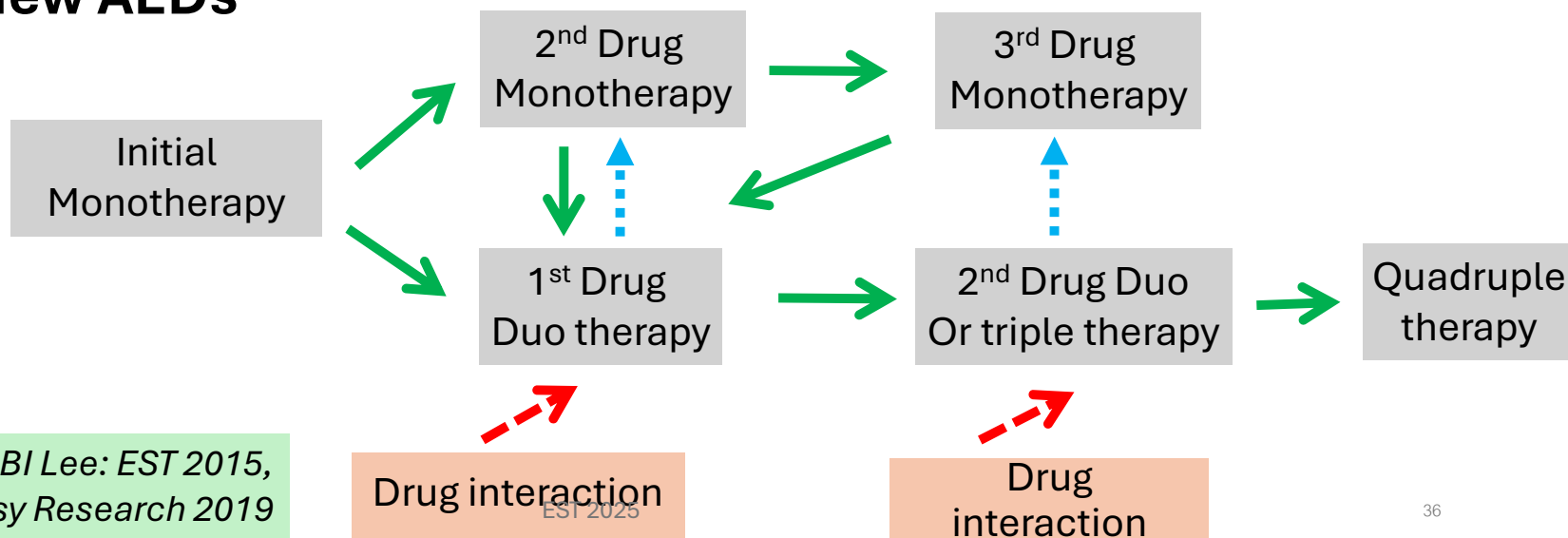


Rational of ASM Treatment

- Era of conventional AED



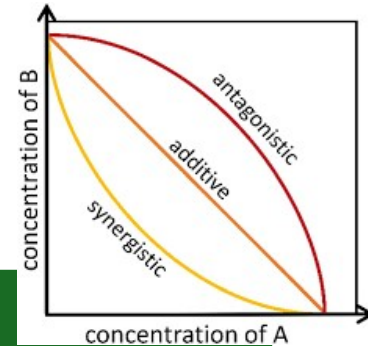
- Era of New AEDs



Modified from Prof BI Lee: EST 2015,
Journal of Epilepsy Research 2019

Combination Regimens

SCB(+) = fast activated
SCB(+) = slow activated



Drug combination

Comment

SCB(+) + SCB(+)

Additive efficacy or antagonism

SCB(+) + SCB(+)

Synergistic efficacy

SCB(+) + Multiple actions

Variable and unpredictable

SCB(+) [or SCB(+)] + Enhanced GABAergic

Synergistic efficacy

Multiple actions + Multiple actions

Synergistic efficacy

LEV(sv2) + Other AEDS (SCB/multiple)

Additive or synergistic efficacy

GBP + Other AEDS

Synergistic efficacy



Practicing Real-life



ASM Selections @ seizure type/syndrome

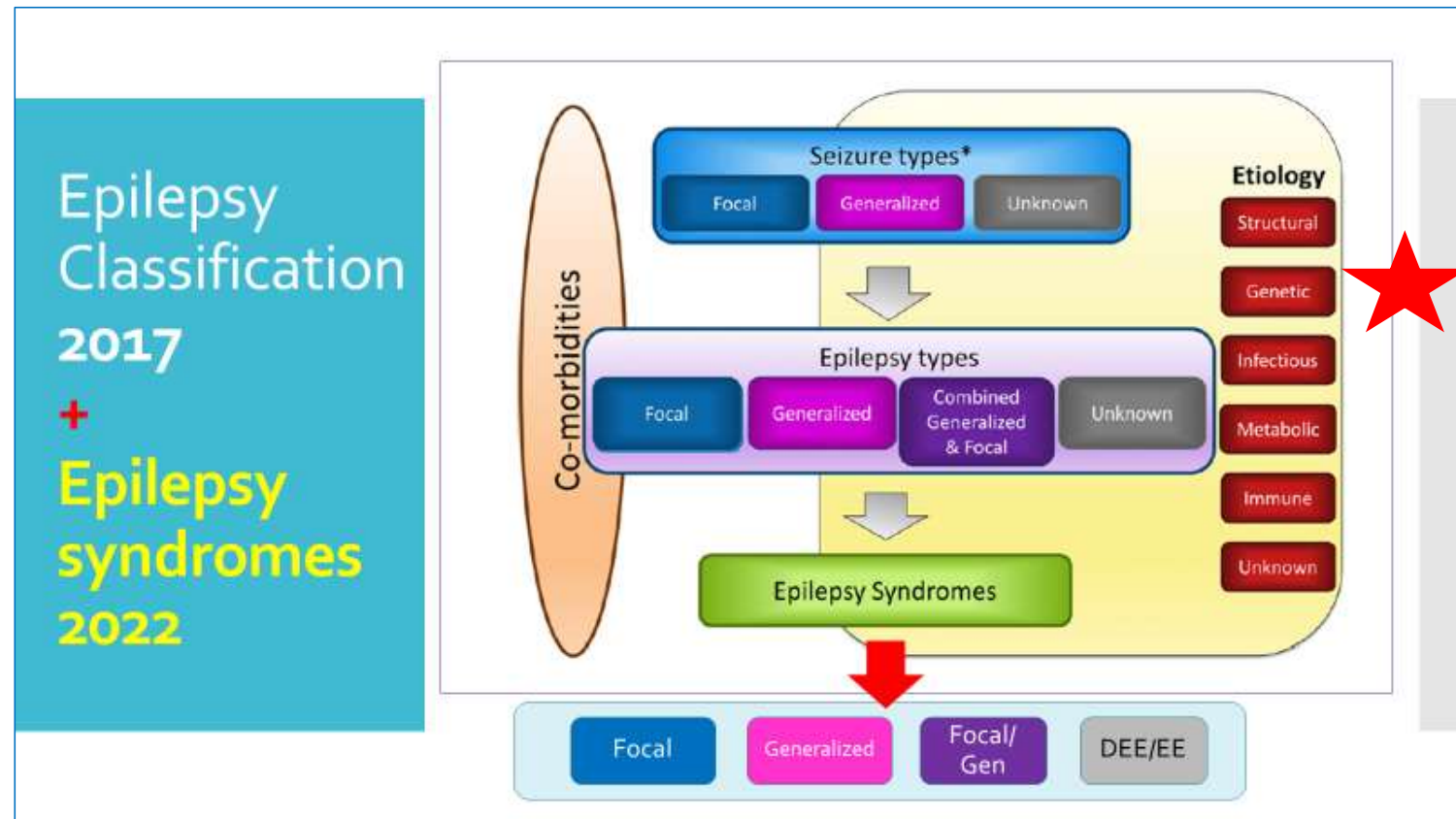
0 Seizure mimicker

1.1 First seizure

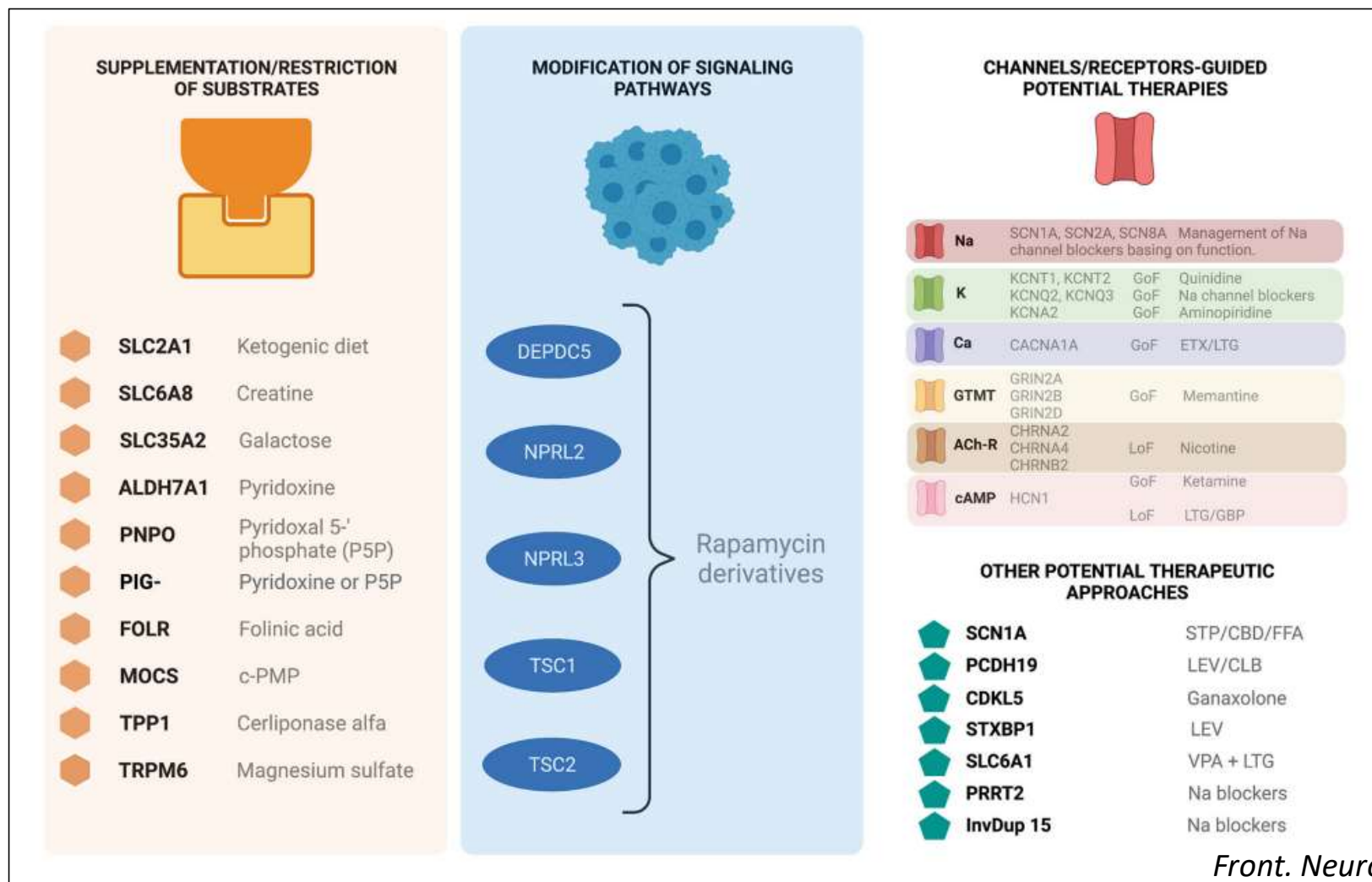
1.2 Epileptic syndrome



ASM Initiation



Genetic background



Treatment in Genetic Epilepsy

	Condition	Gene(s)	Treatment
a. Established treatments	Pyridoxine-dependent epilepsy	<i>ALDH7A1, PROSC</i>	Pyridoxine (vitamin B6)
	Unverricht-Lundborg disease	<i>CSTB</i>	Avoid sodium channel blockers, GABAergic drugs
	<i>POLG</i> -related epilepsy	<i>POLG</i>	Avoid valproate
	Pyridoxal 5'-phosphate dependent epilepsy	<i>PNPO</i>	Pyridoxal 5'-phosphate
	Dravet syndrome, <i>SCN1A</i> -related epilepsy	<i>SCN1A</i>	Avoid sodium channel blockers
	<i>SCN2A</i> -related epilepsy	<i>SCN2A</i>	Phenytoin
	<i>SCN8A</i> -related epilepsy	<i>SCN8A</i>	Phenytoin
	GLUT1 deficiency syndrome	<i>SLC2A1</i>	Ketogenic diet
b. Treatment considerations	Tuberous sclerosis complex	<i>TSC1, TSC2</i>	Vigabatrin for infantile spasms
	<i>GRIN2A</i> -related epilepsy (GOF)	<i>GRIN2A</i>	Memantine
	<i>KCNQ2</i> -related epilepsy (LOF)	<i>KCNQ2</i>	Retigabine (ezogabine)
	<i>KCNT1</i> -related epilepsy (GOF)	<i>KCNT1</i>	Quinidine

GOF gain of function, *LOF* loss of function

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ASMs Discontinuation



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T/F Question

If the patient has been seizure-free while on ASMs, which of the following conditions you can stop ASMs?

1. JME
2. LGS
3. Structural focal epilepsy
4. Epilepsy due to brain malformation
5. Epileptic encephalopathy

Seizure recurrence **vs** Seizure freedom after ASMs discontinuation

Factors associated w an **increased** risk of seizure **recurrence**

- **Long** duration of epilepsy before remission
- **More** than 10 seizures before remission
- Short seizure-free interval before ASM withdrawal
- Older age at onset of epilepsy (in pts >25 yrs)
- History of febrile seizures
- Not a self-limiting epilepsy syndrome
- Developmental delay
- Epileptiform abnormality on EEG before withdrawal

Factors associated w long-term seizure **freedom** (at 10 years after ASM withdrawal)

- **Short** duration of epilepsy before remission
- **Low** number of seizures before remission
- One or low number of ASM before withdrawal
- Long seizure-free interval (years) before ASM withdrawal
- No history of focal seizures
- No epileptiform abnormality on EEG before withdrawal

ASMs Discontinuation Issues

Children	Adult
No difference in sz recurrence between tapering ASMs after 2 or 4 years of seizure freedom	In long-term (24-60 mo) risk of sz recurrence is possibly higher in adults who tapering ASMs after 2 years
Interictal epileptiform activity possibly increases risk of seizure recurrence (low confidence)	
Withdrawal ASMs at a rate of 25% every 10 days-2 weeks or 25% every 2 months has no difference	

Risk Factors for Recurrence of Epileptic Seizures after ASM Withdrawal in **Pediatric patients**

- Generalized non-motor absence seizures: 20-30% relapse
- Focal seizures: 44% relapse (*Focal seizures with diminished awareness have greater risk of relapse*)
- Juvenile myoclonic epilepsy: recurs in 33-78%, only 25-26% can undergo treatment withdrawal
- IESS, Lennox-Gastaut syndrome, and Dravet syndrome have a high risk of recurrence

Other Risk Factors of Seizure Recurrence:

- Symptomatic epilepsies: 41-42% risk
- Neurological anomalies at birth
- Impaired neurodevelopment, intellectual quotient < 70
- ≥ 10 seizures / Prolonged epilepsy before remission
- Average of five seizures per year: 68% relapse
- Prolonged seizures
- Hx of febrile seizures has 2 times the risk of relapse
- Age of onset of epilepsy younger than 2 or older than 12 years old
- EEG with epileptiform activity before withdrawal.

T/F Question

If the patient has been seizure-free while on ASMs, which of the following conditions you can stop ASMs?

1. JME
2. LGS
3. Structural focal epilepsy
4. Epilepsy due to brain malformation
5. Epileptic encephalopathy

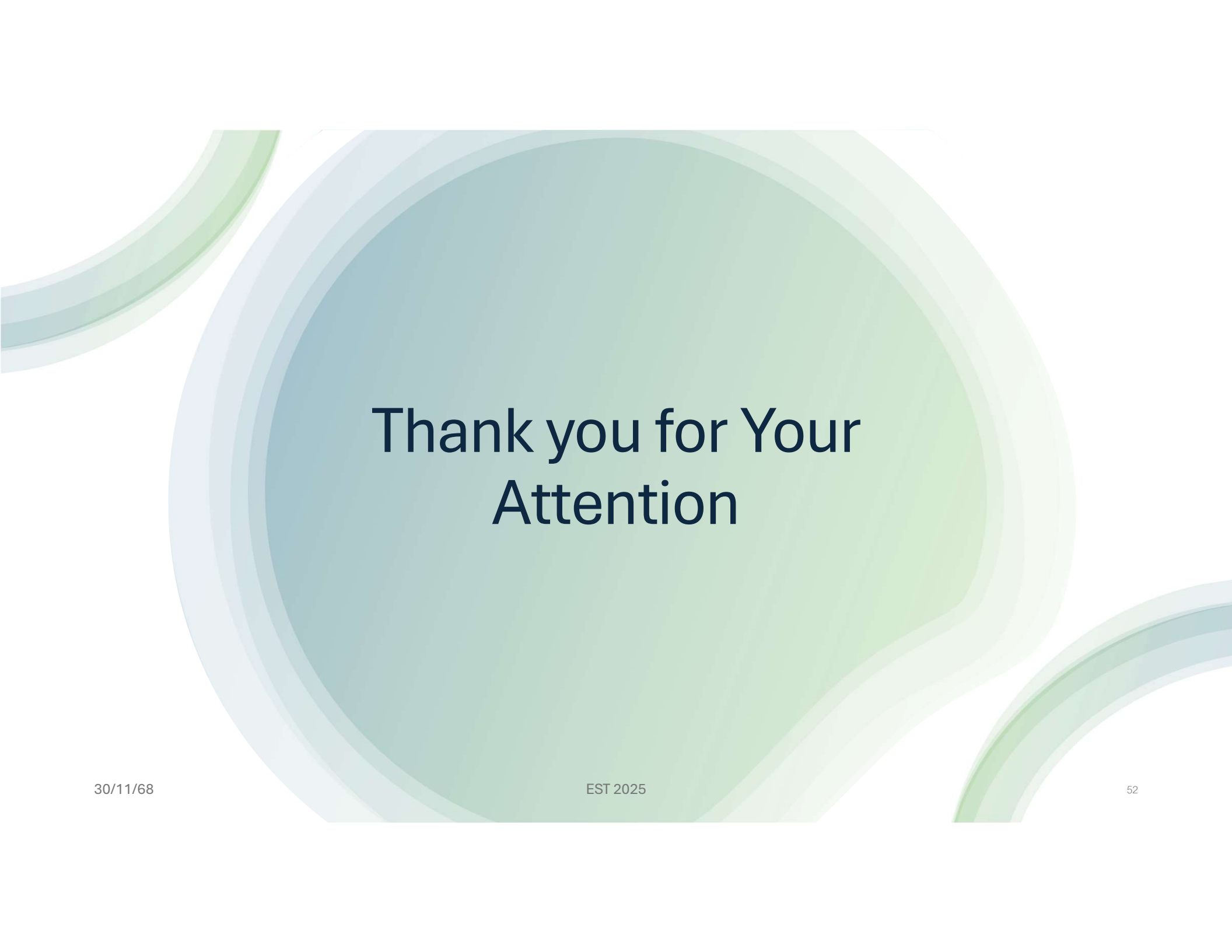
Predictors of Seizure Recurrence post-ASM Withdrawal after Epilepsy Surgery

1. Hx of focal to bilateral T-C seizure
2. Long duration of epilepsy prior to surgery
3. Normal MRI (non lesional)
4. Higher number of ASMs at time of surgery
5. Cortical dysplasia on histopathology
6. Early postoperative seizure (1 week-3 months post Sx)
7. Persistent aura
8. Interictal discharges on postoperative EEG
9. Early ASM tapering

Epilepsy Resolved

- Individual in each patient
- Age-dependent epilepsy syndrome but are now past the applicable age
- Remained seizure-free for the last 10 years, with **no seizure medicines** for the last **5 years**

Epilepsia, 55(4):475–482, 2014



Thank you for Your
Attention