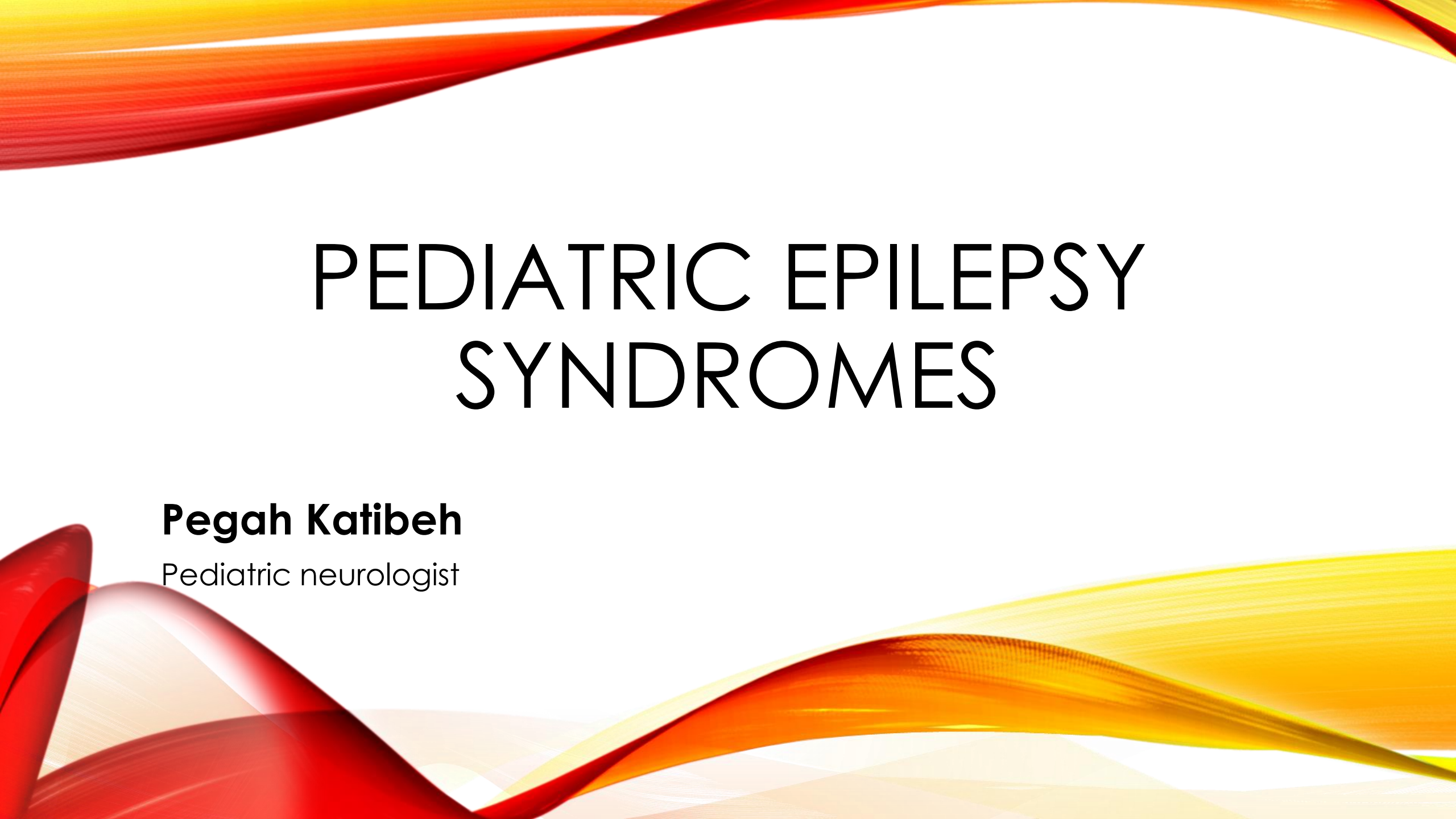




PEDIATRIC EPILEPSY SYNDROMES

Pegah Katibeh

Pediatric neurologist

در ویدیوی زیر که باعث نگرانی شدید مادر این نوزاد شده است چه میبینید؟ جهت درمان چه باید کرد؟



NEONATAL SLEEP MYOCLONUS

- Repetitive, usually bilateral, rhythmic jerks involving the upper and lower limbs during non-rapid eye movement sleep, sometimes mimicking clonic seizures.
- Although not stimulus sensitive, a slow (1-Hz) rocking of the infant in a head-to-toe direction is a specific diagnostic test
- The **lack of autonomic changes**,
occurrence only in sleep,
suppression by awakenings differentiate from epileptic seizures.
- Remission is spontaneous, usually at **2-3 mo** of age.
- In older children and adults, sleep myoclonus consists of random myoclonic jerks of the limbs.

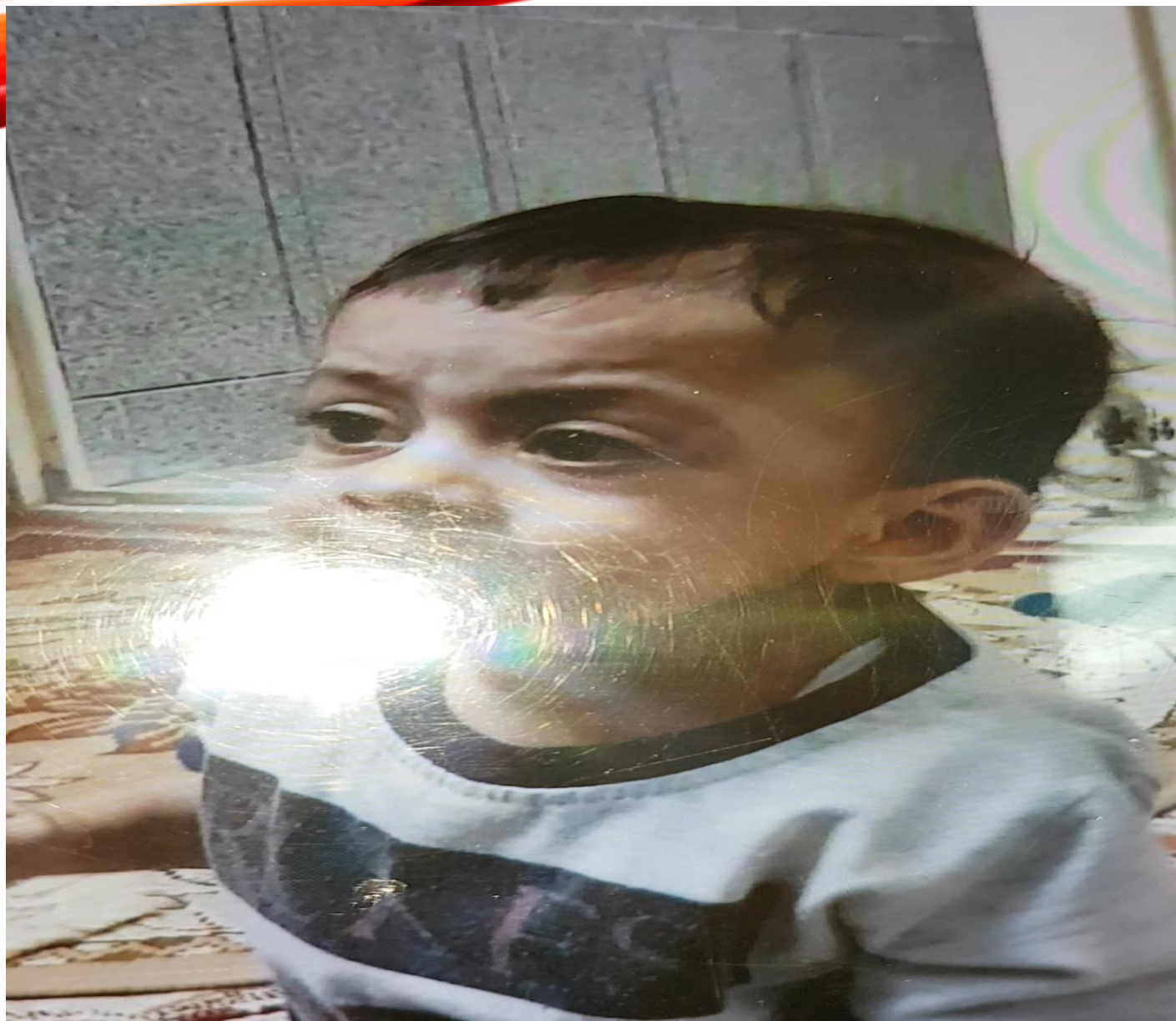


BREATH-HOLDING SPELLS

- a misnomer, because they are not necessarily **self-induced**
- result from the **immaturity of the autonomic** system
- two different forms. The first type, **pallid breath-holding spell**, which is caused by reflex vagal-cardiac bradycardia and asystole.
- The second type is the **cyanotic**, or **blue, breath-holding spell**, which does not occur during inspiration but results from **prolonged expiratory apnea** and intrapulmonary shunting
- Episodes usually start with a cry (often, in the case of the pallid type, a **silent cry** with marked pallor)
- progress to **apnea** and cyanosis.
- Spells usually begin between **6 and 18 mo** of age.
- **Syncope**, **tonic** posturing, and even **reflex anoxic seizures** may follow severe episodes,

- 
- Injury (such as even a **minor bump** on the head), **pain**, and **frustration**, particularly with surprise, are common triggers.
 - There usually is a family history of **vasovagal syncope** or **breath-holding spells**.
 - Education and **reassurance** of the parents is usually all that is needed
 - As a rule, self-limited and are outgrown within a few years.
 - Screening for **anemia** and electrical abnormalities (EKG) rarely **long-QT** syndromes is recommended
 - Anticholinergic drugs (e.g., **atropine** sulfate 0.03 mg/kg/day, in 2-3 divided doses with a maximum daily dose of 1.2 mg),

- Antiseizure (levetiracetam) drug therapy for coexisting anoxic seizures that are recurrent, prolonged, and not responding
- It is important also to educate parents on how to handle more severe spells with first-aid measures or even basic cardiopulmonary resuscitation
- Extremely severe episodes resulting in marked bradycardia and asystole have been reported to respond to a cardiac pacemaker.
- All parents should be taught not to provide secondary gain
- Also, preparation for unpleasant experiences (such as receiving a shot) rather than surprising the child can help.



SHUDDERING ATTACKS

- characterized by **rapid tremors** of the head, shoulder, and trunk, lasting a **few seconds**,
- often associated with **eating**, and recurring many times a day.
- Others have considered shuddering as an **early manifestation** of essential tremor because a family history of **essential tremor** is often present.

مادر این کودک ۳ ساله با شکایت از حرکات غیر طبیعی
به شکل زیر وی را نزد شما آورده است جهت تشخیص و
تایید آن چه می کنید؟



SPASMUS NUTANS

- Triad of **nystagmus**, **head tilt**, and **head nodding**.
- If **diurnal fluctuation** occurs, symptoms may look like those of epileptic seizures.
- A **brain MRI** should be performed because the triad has been associated with masses in the **optic chiasm** and **third ventricle**.
- **Retinal disease** should also be ruled out.
- In the absence of these associations, **remission** occurs before **5** yr of age.





MASTURBATION

- **Infantile gratification** (masturbation)
- which is more common in girls
- usually occurs at 2-3 yr of age
- often associated with perspiration, irregular breathing, and grunting, but no loss of consciousness.
- Occasionally this is associated with child abuse or with other psychopathology.

AGE	SYNCOPE AND OTHER GENERALIZED PAROXYSMS	MOVEMENT DISORDERS AND OTHER ABNORMAL MOVEMENTS	OCULOMOTOR AND VISUAL ABNORMALITIES	SLEEP DISORDERS
Neonate	Apnea Paroxysmal extreme pain disorder	Jitteriness, tremor, increased startle reflex, hiccups Hyperekplexia, paroxysmal dystonic choreoathetosis	Paroxysmal tonic upgaze Alternating hemiplegia of childhood, staring, daydreaming, and time-out "unresponsiveness"	Benign neonatal sleep myoclonus Sleep transition disorders, REM
Infants	Reflex anoxic seizures Breath-holding spells Benign paroxysmal vertigo Paroxysmal extreme pain disorder	Jitteriness Sandifer syndrome Paroxysmal dystonic choreoathetosis Benign myoclonus of early infancy Pathologic startle Shuddering attacks, infantile head atonic attacks Benign paroxysmal torticollis Psychological disorders Alternating hemiplegia of childhood Jactatio capitis (head banging) Drug reactions	Paroxysmal tonic upgaze Oculomotor apraxia Spasmus nutans Opsoclonus-myoclonus syndrome, staring, daydreaming, and time-out "unresponsiveness"	Non-REM partial arousal disorders REM sleep disorders Narcolepsy Sleep transition disorders (somnambulism, somniloquy)
Children and adolescents	Benign paroxysmal vertigo Compulsive Valsalva-like maneuver Familial hemiplegic migraine Syncope (long QT, vasovagal, vagovagal, orthostatic, migraine-induced) Psychogenic seizures Transient global amnesia Hyperventilation spells, factitious disorder	Tics Tremor Pathologic startle Paroxysmal dyskinesias Alternating hemiplegia of childhood Benign paroxysmal torticollis Episodic ataxia Psychological disorders, including factitious disorder imposed on another, malingering Masturbation Psychogenic seizures Cataplexy Jactatio capitis (head banging) Episodic rage, drug reactions, factitious disorder	Staring, daydreaming, and time-out "unresponsiveness" Drug reactions, hallucinations, visual snow Conversion reactions, factitious disorder	Non-REM partial arousal disorders REM sleep disorders Narcolepsy Sleep transition disorders (somnambulism, somniloquy) Sleep myoclonus Restless legs syndrome, conversion reactions, factitious disorder

Seizure Evaluation on First Visit

- 1 Seizure / seizure mimic ?
- 2 Is it unprovoked / provoked seizure?
- 3 Generalized / focal seizure?
- 4 Etiology?
- 5 Any associated comorbidities?
- 6 Treatment received till now?

EPILEPSY CLASSIFICATION

I. E. Scheffer et al.

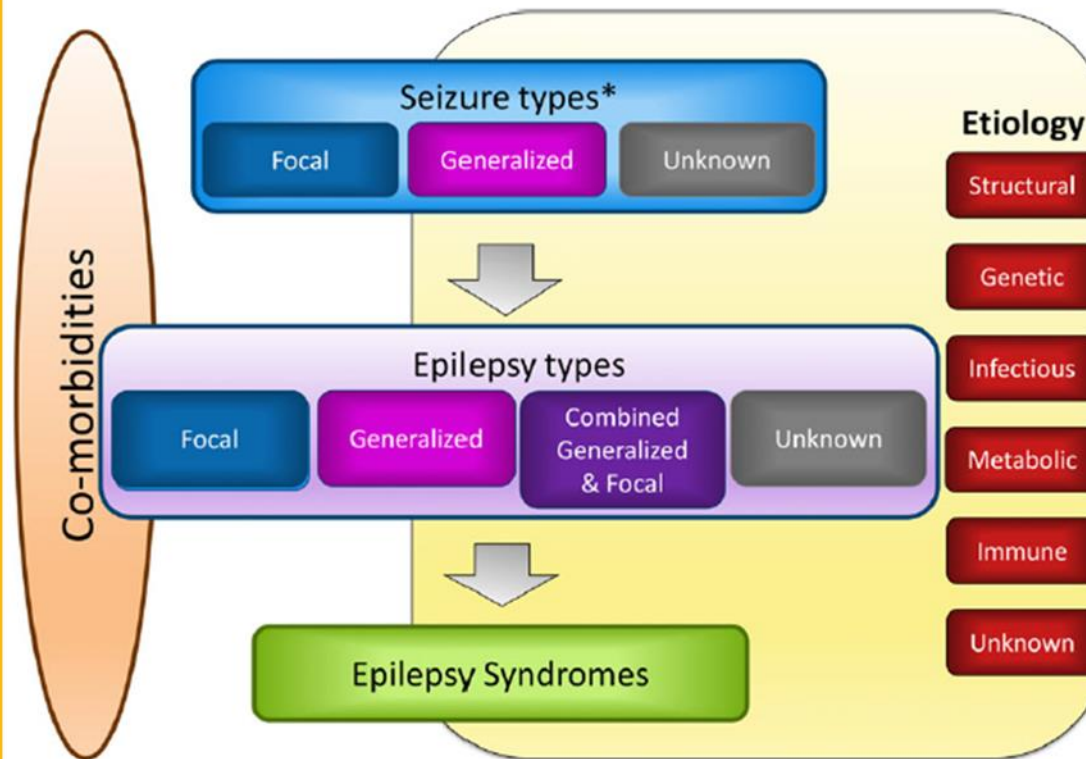
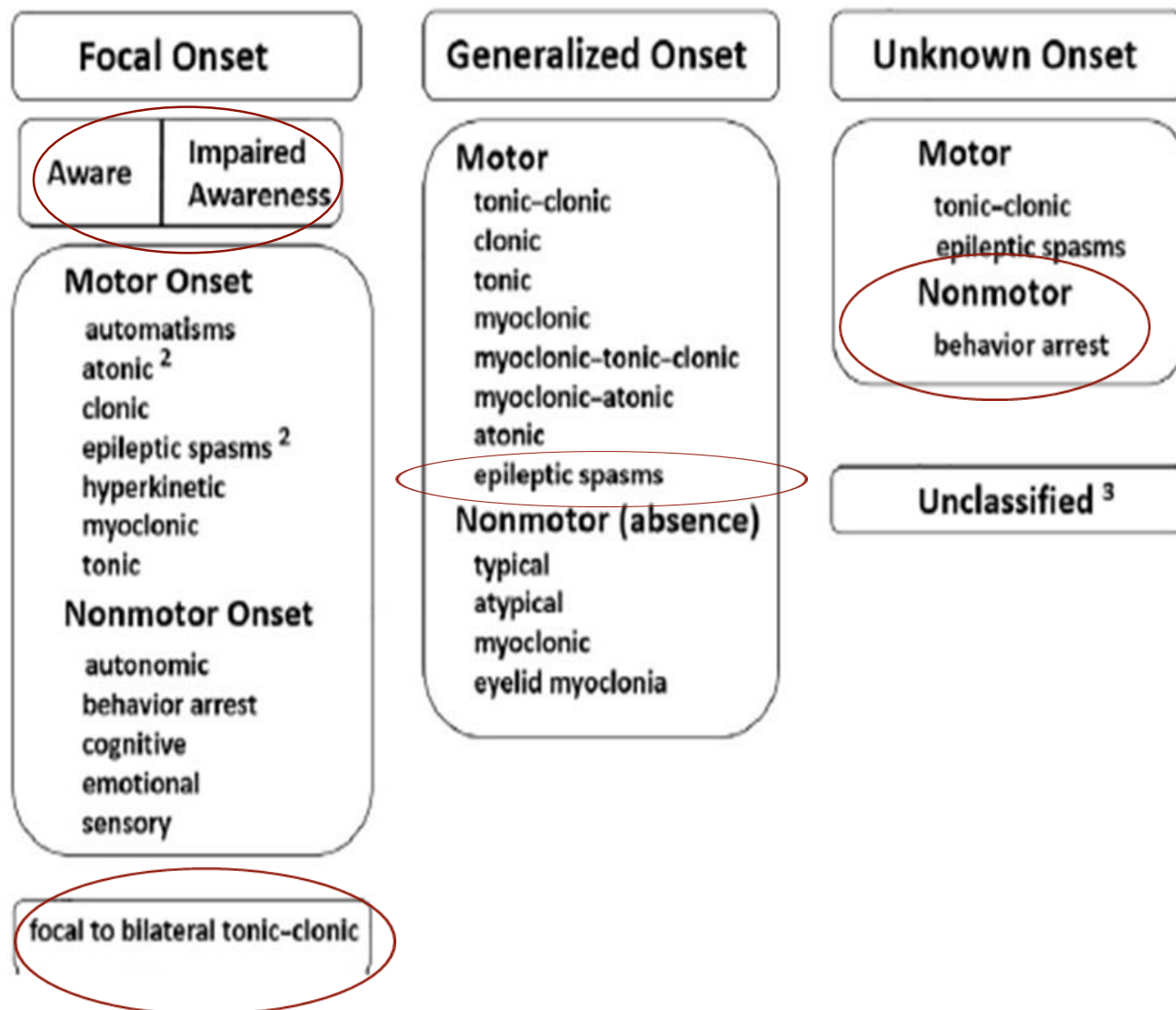


Figure 1. Framework for classification of the epilepsies. *Denotes onset of seizure. *Epilepsia* © ILAE

ILAE 2017 Classification of Seizure Types Expanded Version ¹



ION

GENERALIZED SEIZURES-AFFECT THE ENTIRE BRAIN

- Tonic Clonic (rigid/jerking)
- Absence (starring spell)
- Other motor including:
 - Myoclonic (muscle jerks)
 - Atonic (drop seizure)
 - Epileptic Spasms

FOCAL SEIZURE-AFFECT PART OF THE BRAIN

- Aware:

Alert, involuntary movement, odd taste/smell, fear/happiness, sweating/goose bumps

- Impaired awareness:

Aura, unconscious, lip smacking, meaningless movements, picking at clothing, wandering around, repeating words

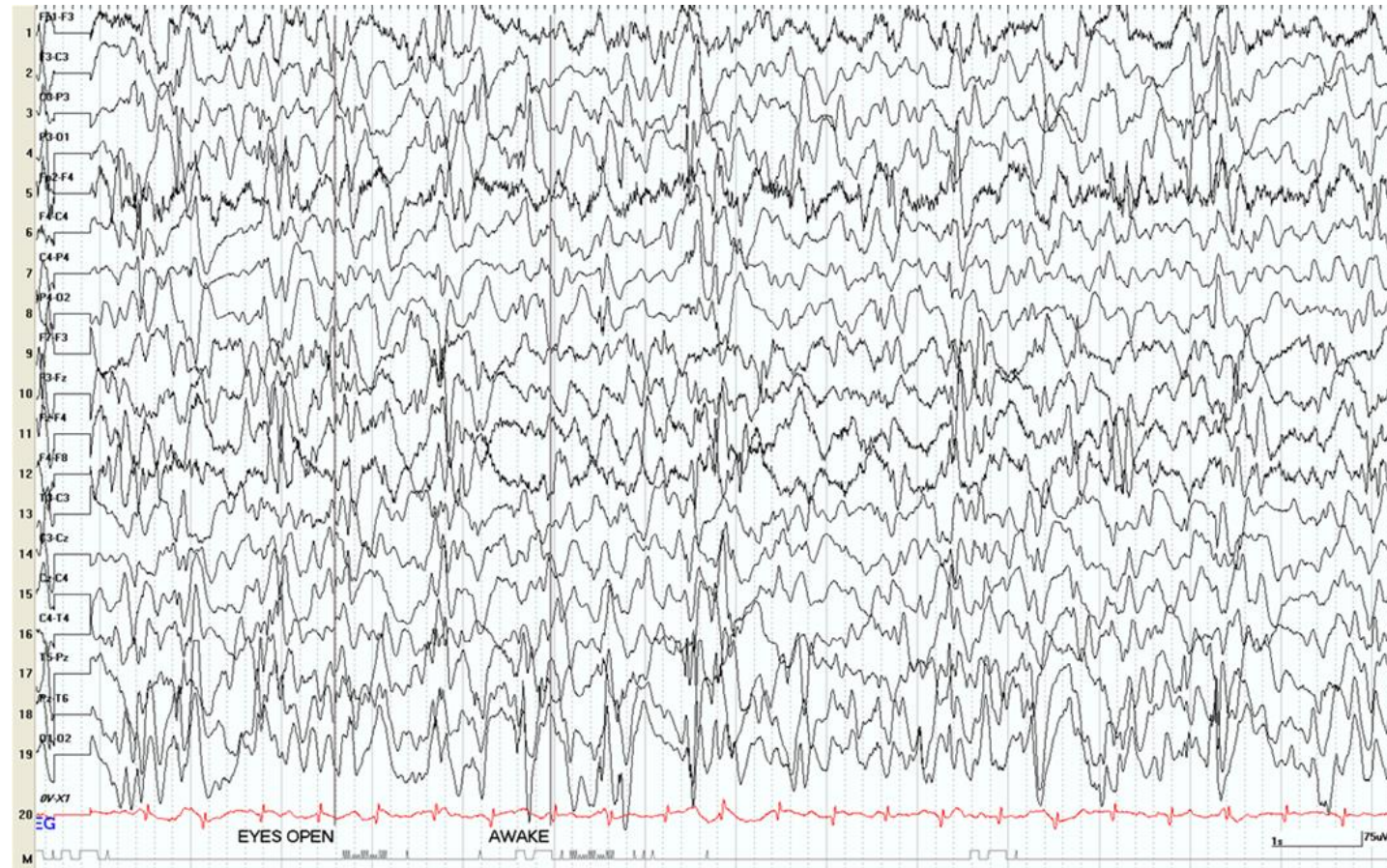
INFANTILE SPASMS

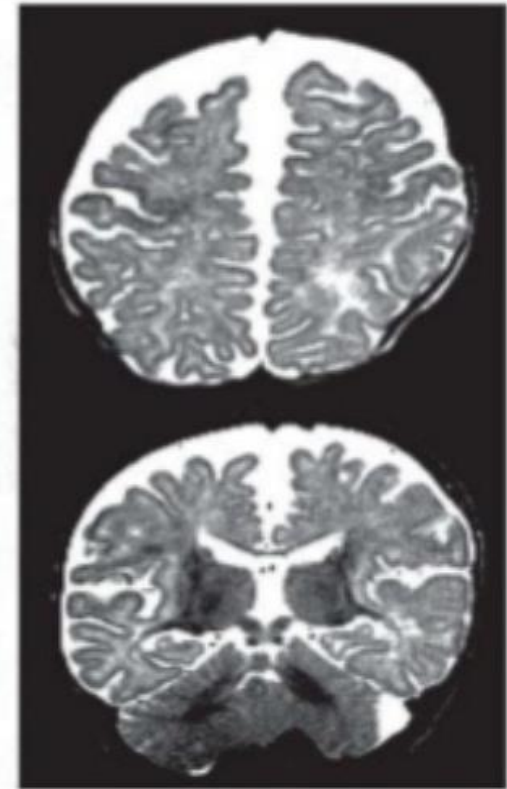
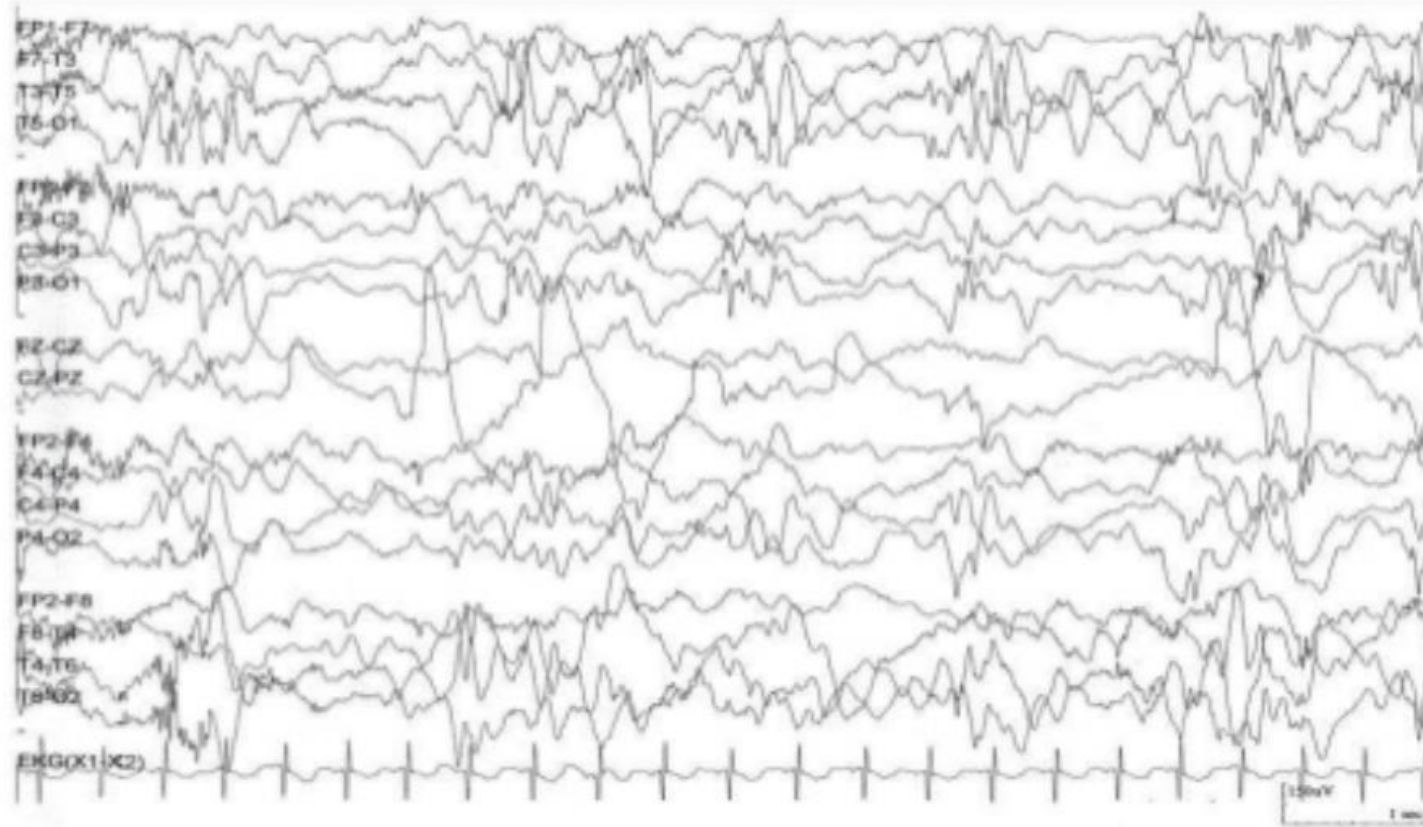
- Clinical – usually trunk flexion and extremity extension in clusters
- 50-60% continue to have seizures (mostly LGS)
- 71-81% MR
- West syndrome = spasms, psychomotor deterioration, and hypsarhythmia
- Tx Corticotropin (ACTH) or high dose steroids, alternatively Vigabatrin

West syndrome

- ▶ Onset before 1 year, peak 4–7 months.
- ▶ Clusters of spasms.
- ▶ Spasms are myoclonic–tonic contractions and can be either flexor, extensor, head or combination.
- ▶ Developmental arrest and psychomotor deterioration.
- ▶ Hypsarrhythmia interictal EEG pattern.
- ▶ Often refractory to antiepileptic therapies.

HYP SARHYTHMIA





EEG showing hypsarrhythmia



Lennox Gastaut syndrome

- ▶ Defined as syndrome characterised by multiple type of seizures including a nucleus of brief tonic or atonic seizures, absence seizures, myoclonic jerks(less common).
- ▶ Interictal EEG pattern of diffuse slow(less than 2.5 hz) spike and wave complexes.
- ▶ Mental retardation common(90%).
- ▶ Non convulsive status epilepticus common.

Lennox Gastaut syndrome

- ▶ More common in males
- ▶ Peak age of onset between 3–5 yrs
- ▶ More frequent during sleep
- ▶ Two thirds to three-fourths–secondary or symptomatic
- ▶ Cortical malformations– B/L perisylvian and central dysplasia, diffuse subcortical laminar heterotopias, focal cortical dysplasia.

Lennox Gastaut syndrome

- ▶ **Atypical absence seizures**– 13 to 100%
- ▶ Burst of spike-wave of 2.5 hz or less seen.
- ▶ Not precipitated by hyperventilation or photic.
- ▶ **Myoclonic**– less common
- ▶ **Atonic seizures**–26–56%
- ▶ Non convulsive status epilepticus–50–75%
- ▶ Consist of subcontinuous atypical absence periodically interrupted by brief tonic seizures.

Lennox Gastaut syndrome

► Predictors of Prognosis

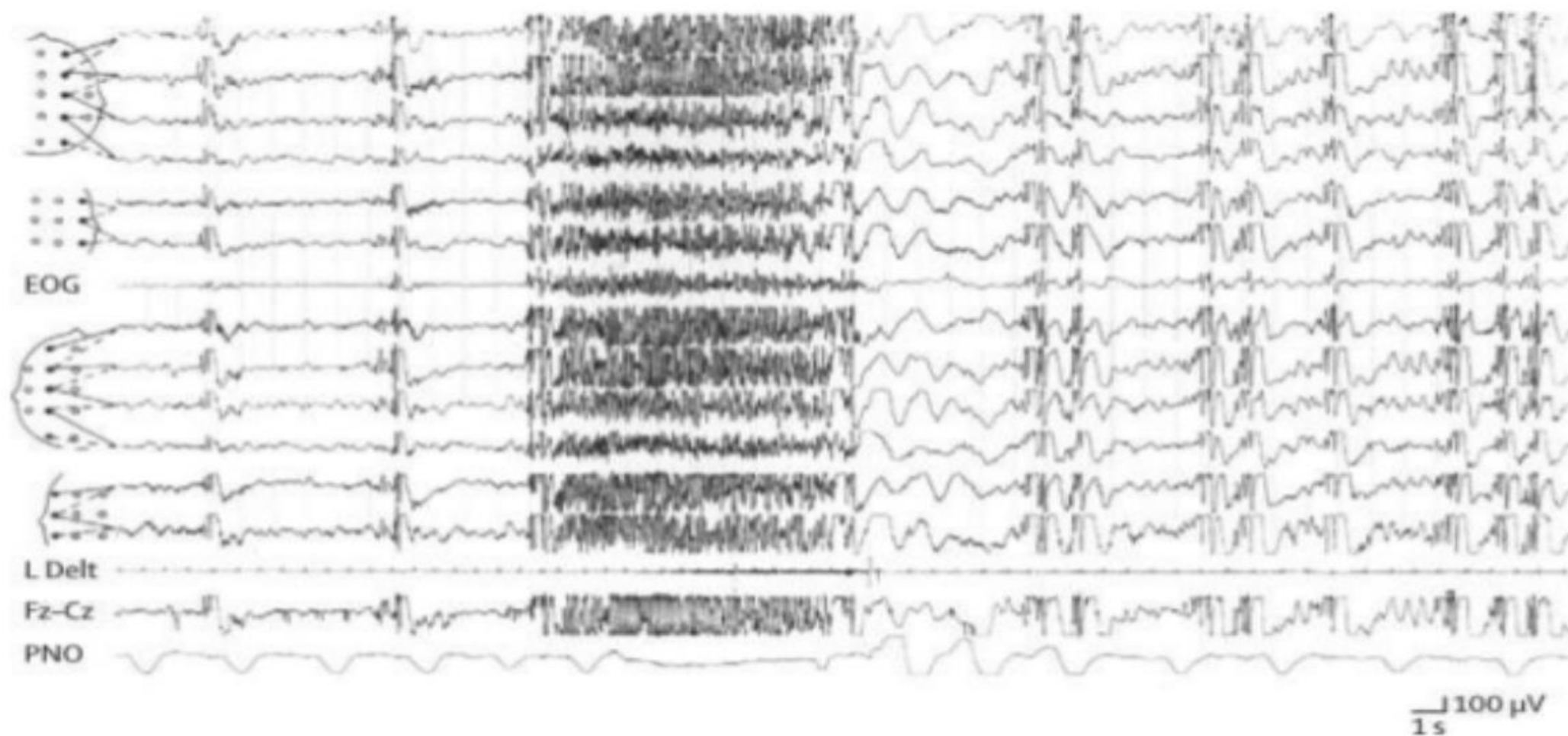
1. Age of onset
2. Frequency of tonic seizures
3. Repeated episodes of non convulsive status
4. Constant slow EEG background.

Lennox Gastaut syndrome

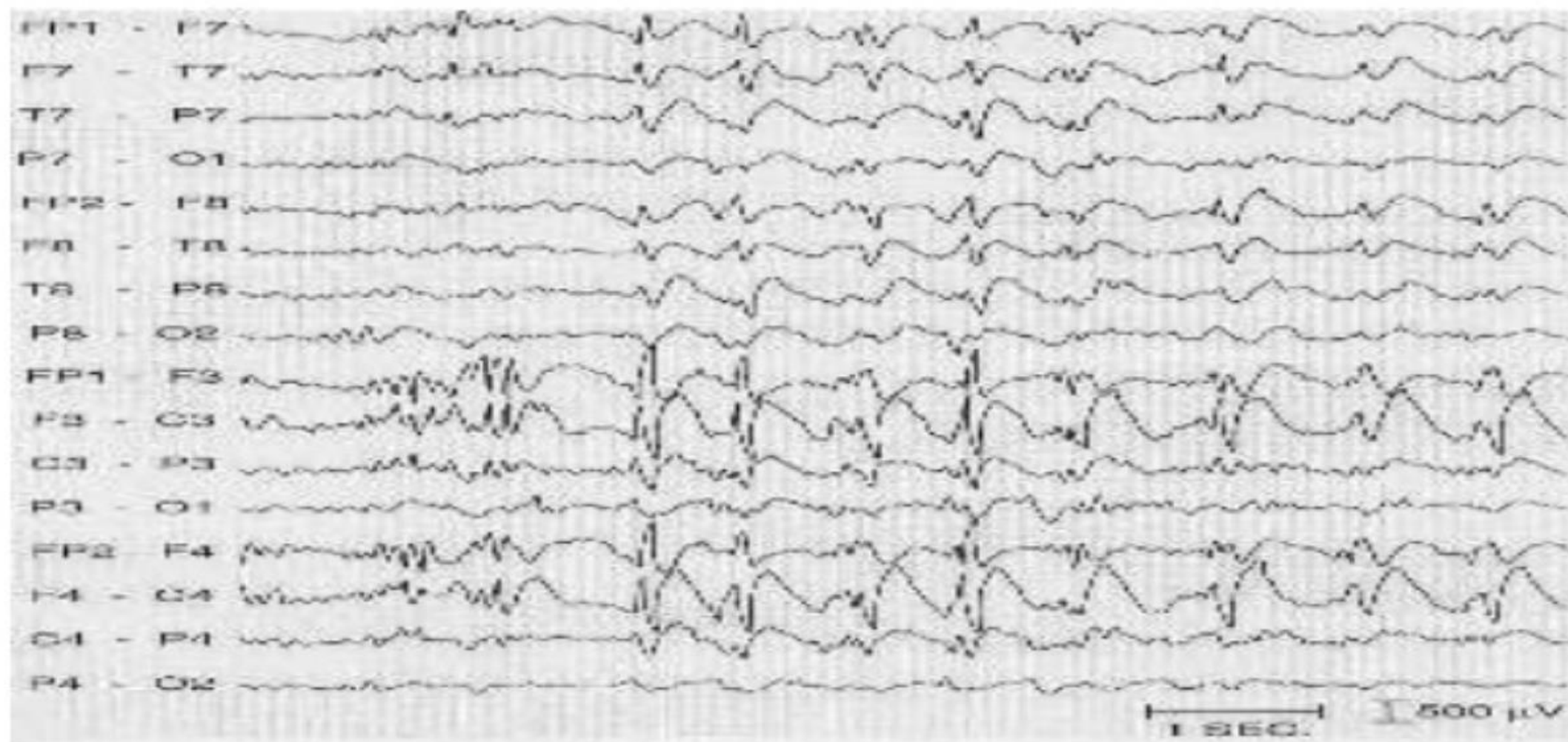
► Treatment

► Refractory to treatment

1. AED–Benzodiazapines, Sodium valproate, Felbamate, Lamotrigine, Topiramate
2. Ketogenic diet
3. Vagal nerve stimulation
4. Surgical resection



Discharge of high amplitude fast rhythms lasting for about 10 secs followed by Polyspikes and spike and wave complex



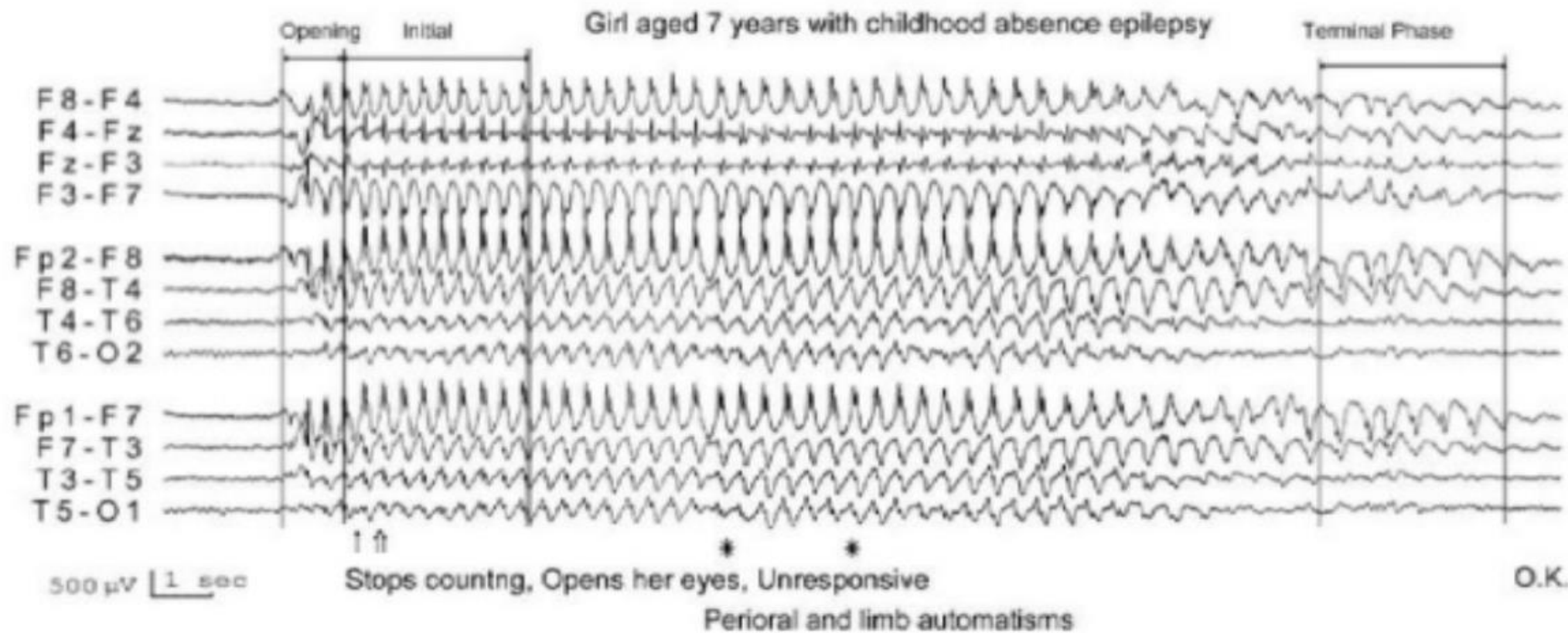
EEG showing spike-wave of 2.5 hz or less.

ABSENCE SEIZURES

- Staring spells
- <30-40 seconds
- No post-ictal
- Multiple per day
- 3 Hz spike-wave
- Can be triggered by hyperventilation

Childhood absence epilepsy (CAE)

- ▶ Also called “pyknolepsy”
- ▶ Onset between 4 and 10 years in a previously healthy child.
- ▶ Frequent typical absence seizures.
- ▶ Maintenance of neurological status and development during course of epilepsy.
- ▶ Ictal EEG: generalized, high-amplitude 3 Hz spike and slow-wave complexes, lasting 4–20 s.
- ▶ Generally responsive to antiepileptic drug (AED) usually with ethosuximide or valproate.
- ▶ One-half of patients develop convulsive seizures, associated with a worse prognosis.



JUVENILE MYOCLONIC EPILEPSY

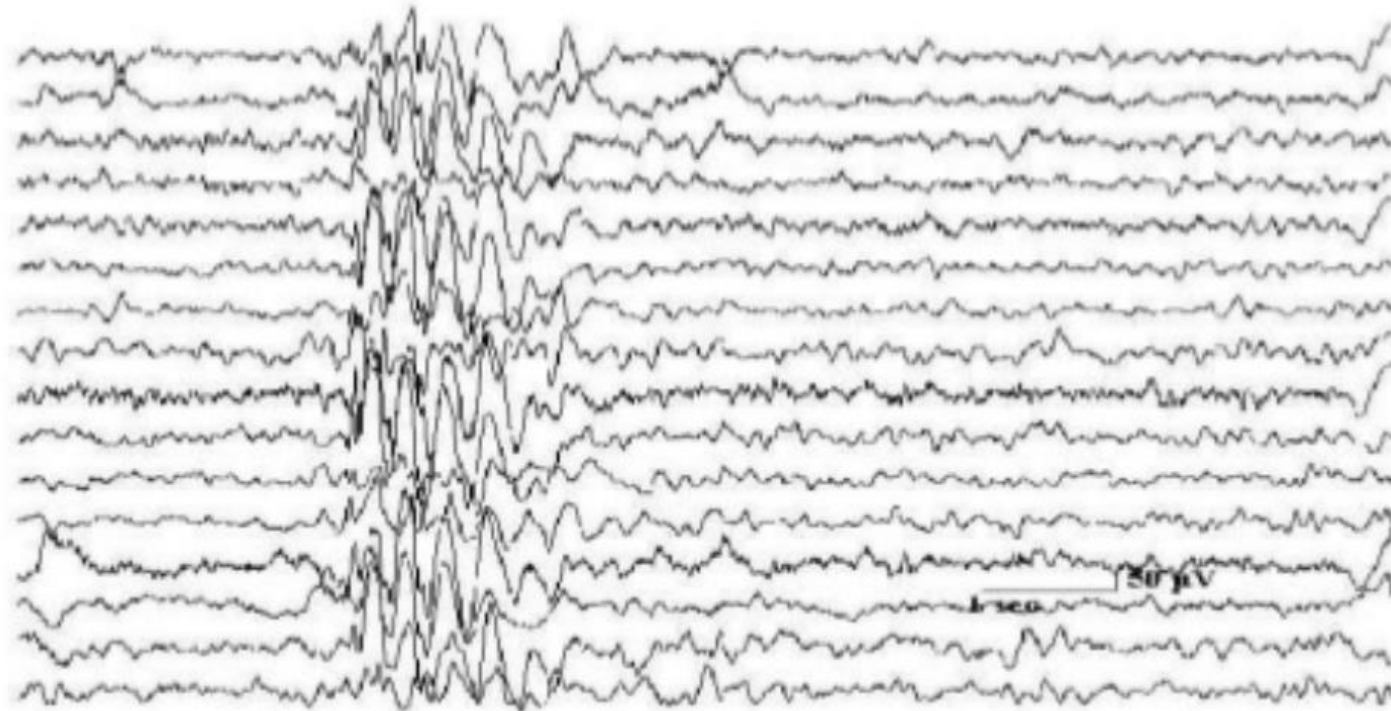
- Most common generalized epilepsy in adolescents
- Myoclonic, absence, and GTC seizures usually after morning awakening, provoked by sleep deprivation, alcohol
- Myoclonic jerks necessary for diagnosis, predominate in upper limbs
- 4-5 Hz generalized polyspike and slow wave discharges; photosensitive
- Most easily treated; 16% pharmacoresistant

Juvenile myoclonic epilepsy (JME)

- ▶ Onset 8 to 26 years (peak 12–18, mean 14 years).
- ▶ Bilateral myoclonic jerks, most frequently upon awakening.
- ▶ Secondary seizure types including GTCS and typical absence seizures.
- ▶ Ictal EEG with generalized high-amplitude polyspike-and-wave.
- ▶ Usually demonstrate a life-long predisposition to generalized seizures.

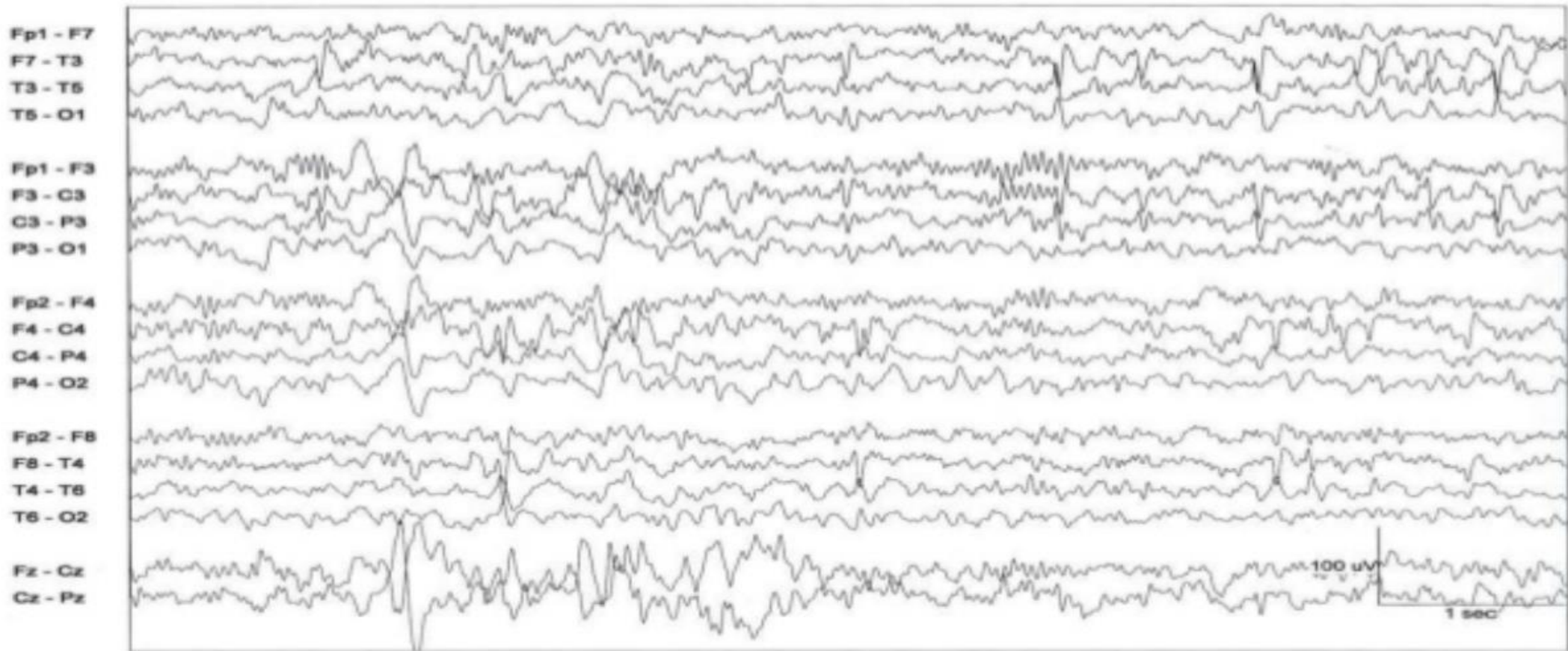
Polyspike and wave discharges seen in juvenile myoclonic epilepsy

FP1-F7
F7-T3
T3-T5
T5-O1
FP1-F3
F3-C3
C3-P3
P3-O1
FP2-F4
F4-C4
C4-P4
P4-O2
FP2-F8
F8-T4
T4-T6
T6-O2



BENIGN EPILEPSY WITH CENTROTEMPORAL SPIKES (BECTS)

- Onset 3-14 years old; most outgrow by 16 years
- Most common focal childhood epilepsy
- Seizures from rolandic cortex
- 80% have < 6 seizures
- Classically, unilateral face, tongue, and/or hand/arm clonic jerking/ parasthesia in early morning or while asleep – may be on either side; often retained awareness but expressive aphasia in ictal/ post-ictal phase
- Seizures may generalize
- Central-temporal spikes, activated by drowsiness/ sleep



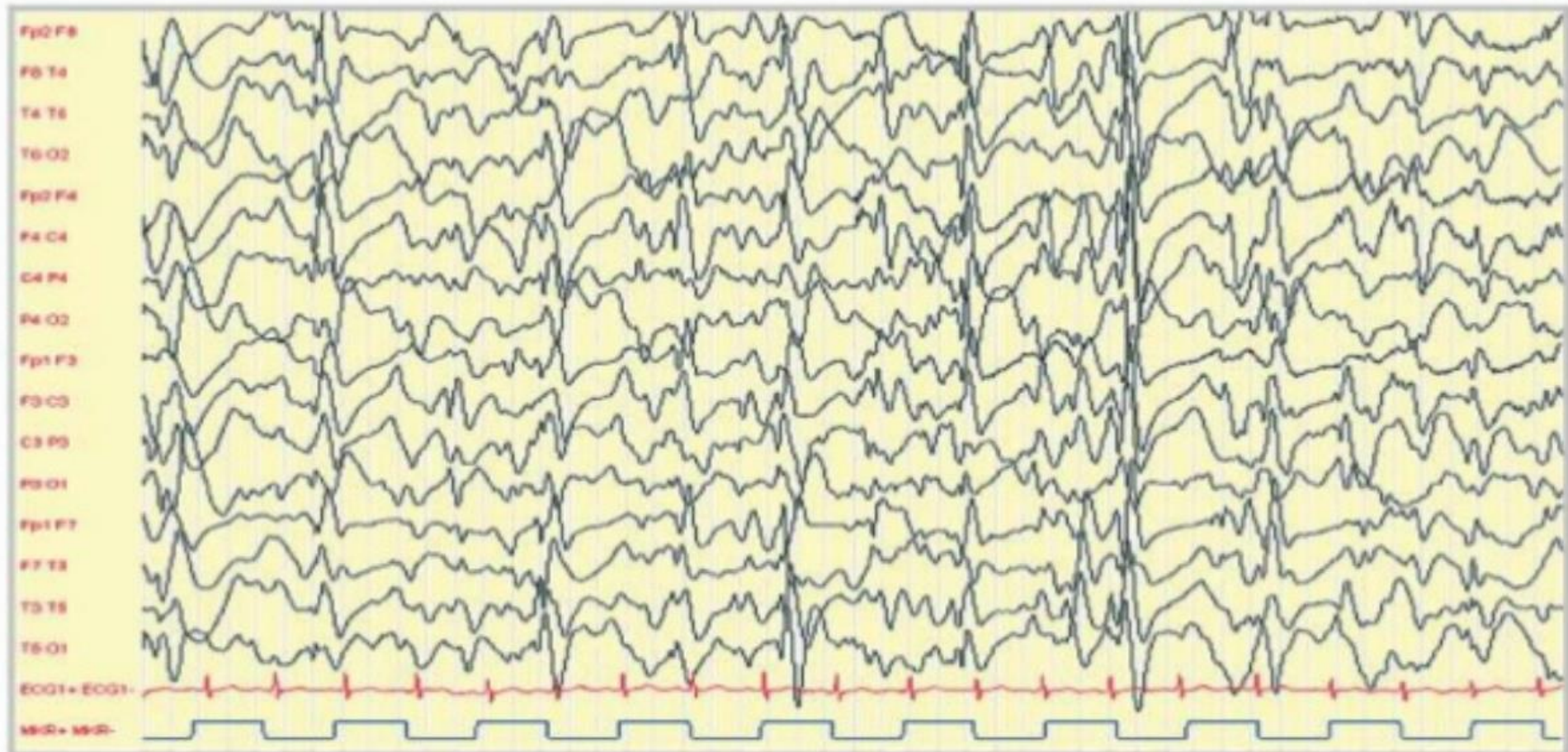
EEG during drowsiness and sleep showing frequent bilateral synchronous/independent biphasic spikes followed by slow waves in the centro-temporal regions.

Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)

- ▶ Childhood onset (peak 4–7 years).
- ▶ Various generalized and focal seizures.
- ▶ Cognitive deterioration and behavioral disturbances.
- ▶ EEG with continuous spike and slow wave seen in at least 85% of slow-wave sleep.
- ▶ Characterized by a hallmark EEG presentation, called continuous spike and-wave during sleep (CSWS) or electrical status epilepticus of slow-wave sleep (ESES) accompanied by seizure activity and neuropsychological deficits.

Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)

- ▶ 2–5 years after seizure onset, CSWS pattern emerges & is temporally associated with emergence of neuropsychological and behavioral disturbances as well as onset of atypical absence seizures in wakefulness.
- ▶ No associated brain pathology
- ▶ Typically some improvement in neurological status once epileptiform activity has resolved.



EEG showing continuous spike and-wave during sleep (CSWS) or electrical status epilepticus of slow-wave sleep.

Landau-Kleffner syndrome (LKS)

- ▶ Onset between 3 and 8 years (peak 5–7 years).
- ▶ Acquired aphasia (verbal auditory agnosia).
- ▶ Continuous spike and wave discharges on EEG, activated in sleep.
- ▶ Resolution of EEG abnormalities in adolescence.
- ▶ Deterioration or significant fluctuation in language are indications to evaluate for LKS.
- ▶ Generalized or focal seizures occur in up to 80% of children and may precede or follow the onset of aphasia
- ▶ Seizures commonly resolve before age 15 years
- ▶ Neuropsychological deficits tend to persist.
- ▶ many epileptologists consider CSWS and LKS on a common syndromic spectrum and consider LKS a specific presentation of epilepsy with CSWS

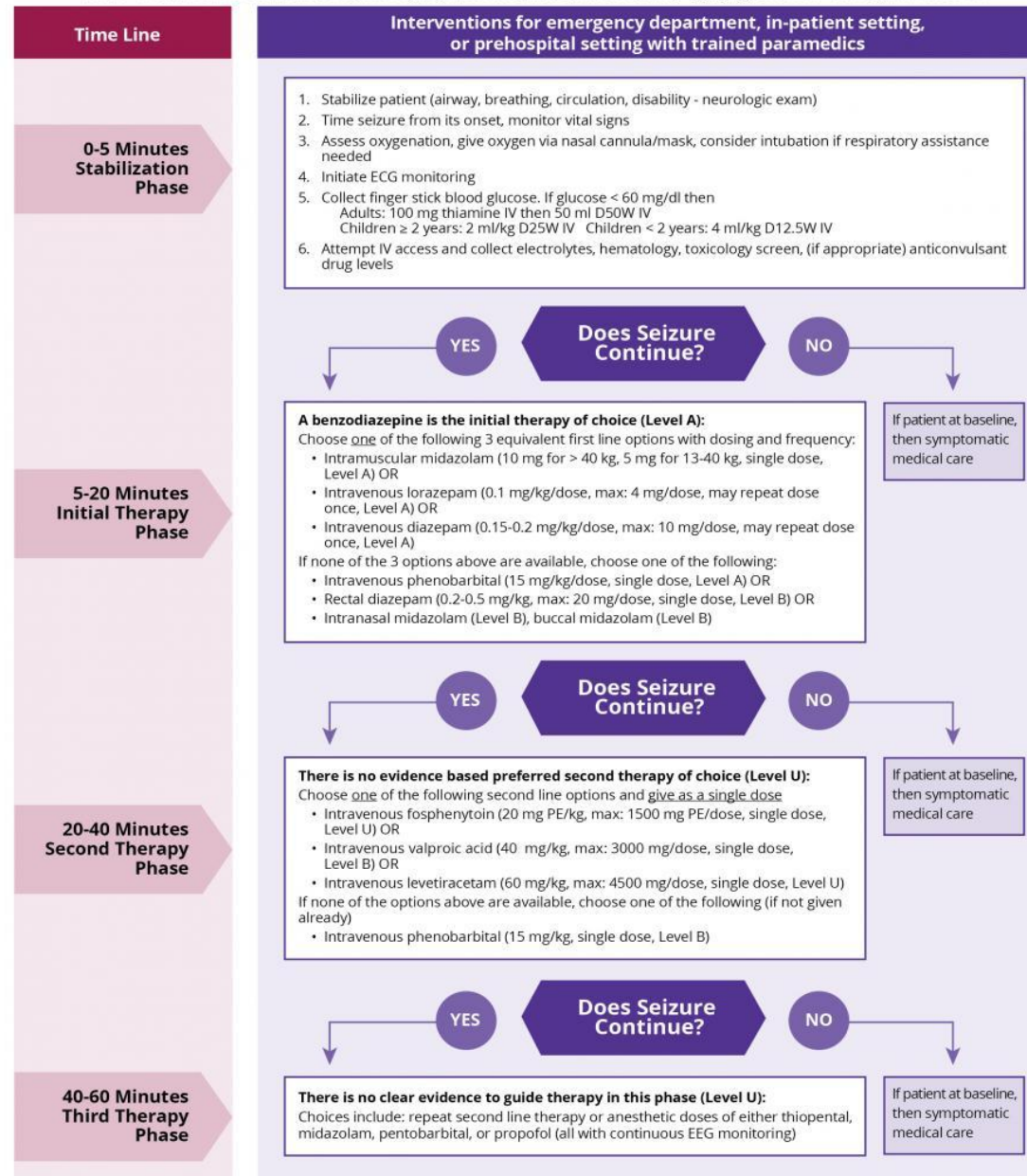
PSEUDO-SEIZURE

- Also known as: psychogenic non-epileptic seizures (PNES), conversion disorder, functional neurologic disorder
- A non-epileptic seizure: no abnormal electrical activity in the brain correlating with the event
- Tx: Cognitive behavioral therapy, psychiatric evaluation, PT/OT

کودک پنج ساله ای را در حال تشنج نزد شما آورده است به گفته
در بدو ورود دستیار .مادر شروع تشنجات در منزل بوده است
کشیک در اتاق احیا به پرستار دستور تزریق میدازولام
عضلانی داده است به نظر شما کار درستی صورت گرفته
است؟

Proposed Algorithm for Convulsive Status Epilepticus

From "Treatment of Convulsive Status Epilepticus in Children and Adults," *Epilepsy Currents* 16.1 - Jan/Feb 2016



STATUS EPILEPTICUS

- Single seizure ≥ 30 minutes
- Multiple seizures without regaining consciousness
- Impending status epilepticus (Chen JWY and Wasterlain CG, 2006) or early status epilepticus (Shorvon S, 2001) = 5 minutes
- Status epilepticus:
 - Convulsive
 - Non-convulsive
- Incidence 20 episodes per 100,000 per patient-year
- 1/3-1/2 present with SE as their first seizure

STATUS EPILEPTICUS

- SE is a medical **emergency**
- requires initial and continuous attention to securing the **airway**, **breathing**, and **circulation** (with continuous monitoring of vital signs including **ECG**)
- determination and management of the underlying **etiology** (e.g., hypoglycemia).
- Laboratory studies: **glucose, sodium, calcium, magnesium, complete blood count, basic metabolic panel, CT scan, and continuous EEG**, are needed for all patients.
- **Blood and spinal fluid cultures, toxic drug screens, and tests for inborn errors of metabolism** are often needed.

- **AED levels** in all patients known already to be taking these drugs.
- EEG to rule out **pseudo–status epilepticus** (psychological **conversion** reaction mimicking SE) or other movement disorders (**chorea, tics**), rigors, **clonus** with stimulation, and **decerebrate/decorticate posturing**.
- EEG helpful in identifying the **type** of SE (generalized vs focal),
- EEG to distinguish between **postictal depression and later stages of SE** in which the clinical manifestations are subtle (e.g., minimal myoclonic jerks) or absent (electroclinical dissociation), esp in paralyzed and intubated patients.

- **Neuroimaging** after the child has been stabilized, especially in asymmetric or focal EEG , or unknown underlying etiology.
- The initial emergent therapy should be started for convulsive seizures lasting **longer than 5 min** and involves the use of a benzodiazepine medication
- **intravenous lorazepam, intravenous diazepam, or intramuscular midazolam** as a first-line agent.
- **intravenous lorazepam** as a **first-line** agent and, if the patient does not have intravenous access, using intramuscular midazolam.
- Other options :buccal or intranasal midazolam, intranasal lorazepam, or rectal diazepam.
- **respiratory depression** is a potential side effect
- If seizures persist 5 min, a **second dose** of the drug should be given.

- Less evidence supports the use of **phenytoin/fosphenytoin, phenobarbital, valproate, or levetiracetam** as alternative **first-line** agents.
- in some infants, a trial of **pyridoxine** may be warranted.
- If persistent seizures **5 min after the second benzodiazepine** dose, fosphenytoin, valproate, or levetiracetam is the recommended option
- Fosphenytoin is given at a loading dose of 20 PE/kg and a level is usually taken 2 hr later to ensure achievement of a therapeutic concentration.
- Depending on the level and response, a maintenance dose can be started **right away** or, more commonly, **6 hr** following the initial bolus.

- Valproate is loading dose of 20-40 mg/kg, should be avoided in patients younger than 2 yr of age and hepatic dysfunction or mitochondrial disease.
- Levetiracetam loading doses of 30-60 mg/kg and is well tolerated, although less data are available regarding its efficacy.
- Intravenous phenobarbital is an alternative option if valproate, fosphenytoin, or levetiracetam is not available
- Not recommended as a first-line urgent therapy (side effects).
- The phenobarbital dose in neonates usually 20 mg/kg loading dose, but in infants and children the dose is often lower to avoid respiratory depression, repeated if no adequate response

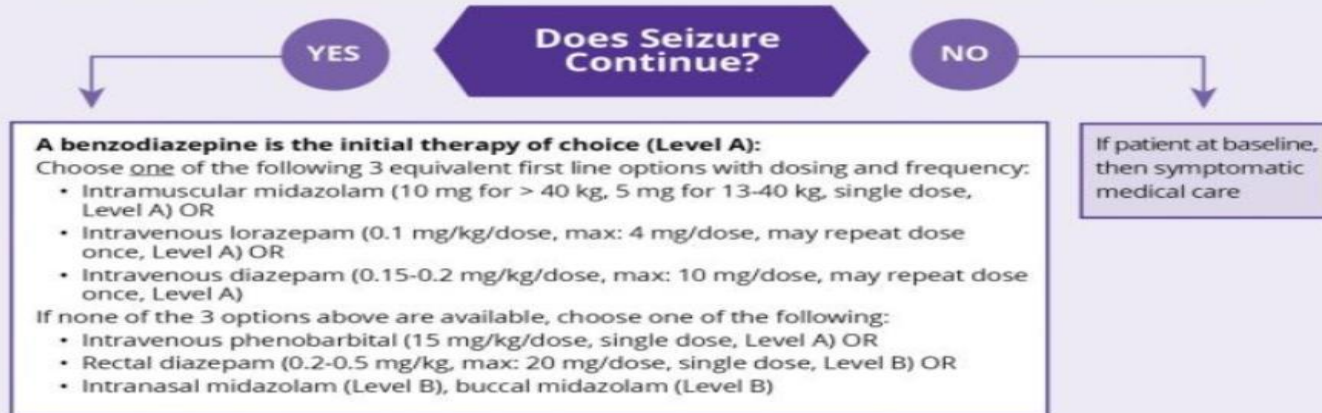
- 
- Pentobarbital coma sometimes needs multiple vasopressors to maintain **blood pressure** during therapy.
 - The choice depends on the experience of the specific center.
 - **Midazolam** probably has fewer side effects but is **less** effective,
 - **Barbiturate** coma is **more effective** but carries a higher risk of side effects.
 - **Propofol** infusion syndrome with lactic acidosis, hemodynamic instability, and rhabdomyolysis with higher infusion rates limiting its use.
 - Electrolytes, CPK, and organ function need to be monitored

- 
- **Ketogenic diet** has also been found to be effective in children, although the response may take up to **a week** following diet initiation
 - ketosis difficult in patient receiving pentobarbital, which has a carbohydrate-rich carrier fluid.
 - Immunotherapy with intravenous **steroids**, **immunoglobulins**, and/or **plasma exchange** is often used in cases of unclear etiology
 - In **anti-NMDA receptor encephalitis** or **CNS vasculitis**, immunotherapy may be the first-line therapy.
 - **Inhaled anesthetics** such as **isoflurane** require an anesthesiologist
 - **Induced hypothermia** has also been used

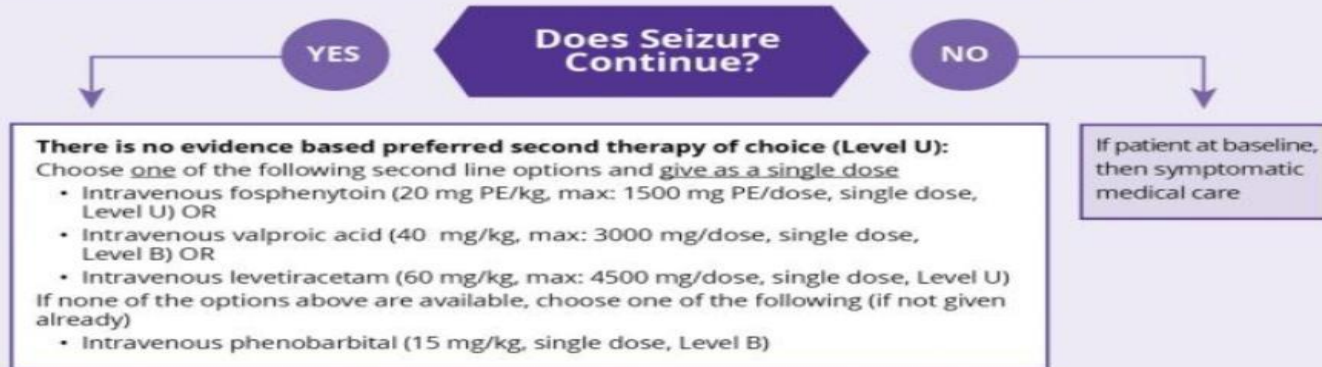
**0-5 Minutes
Stabilization
Phase**

1. Stabilize patient (airway, breathing, circulation, disability - neurologic exam)
2. Time seizure from its onset, monitor vital signs
3. Assess oxygenation, give oxygen via nasal cannula/mask, consider intubation if respiratory assistance needed
4. Initiate ECG monitoring
5. Collect finger stick blood glucose. If glucose < 60 mg/dl then
Adults: 100 mg thiamine IV then 50 ml D50W IV
Children ≥ 2 years: 2 ml/kg D25W IV Children < 2 years: 4 ml/kg D12.5W IV
6. Attempt IV access and collect electrolytes, hematology, toxicology screen, (if appropriate) anticonvulsant drug levels

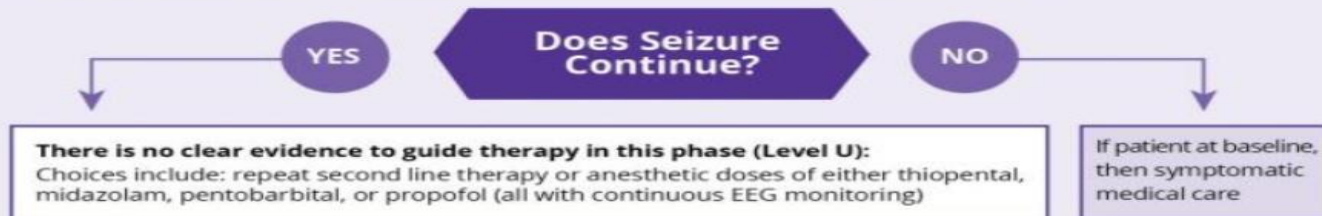
**5-20 Minutes
Initial Therapy
Phase**



**20-40 Minutes
Second Therapy
Phase**



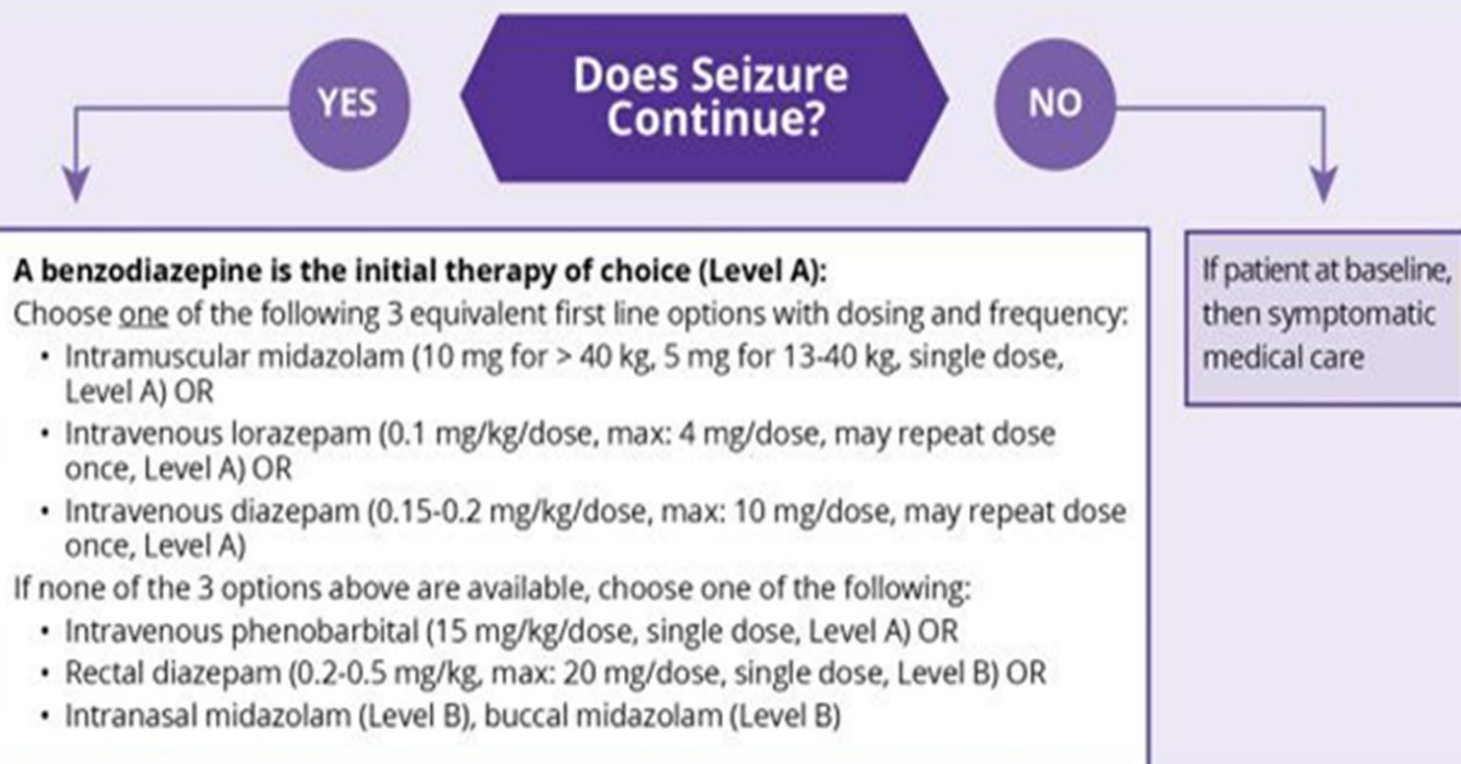
**40-60 Minutes
Third Therapy
Phase**



**0-5 Minutes
Stabilization
Phase**

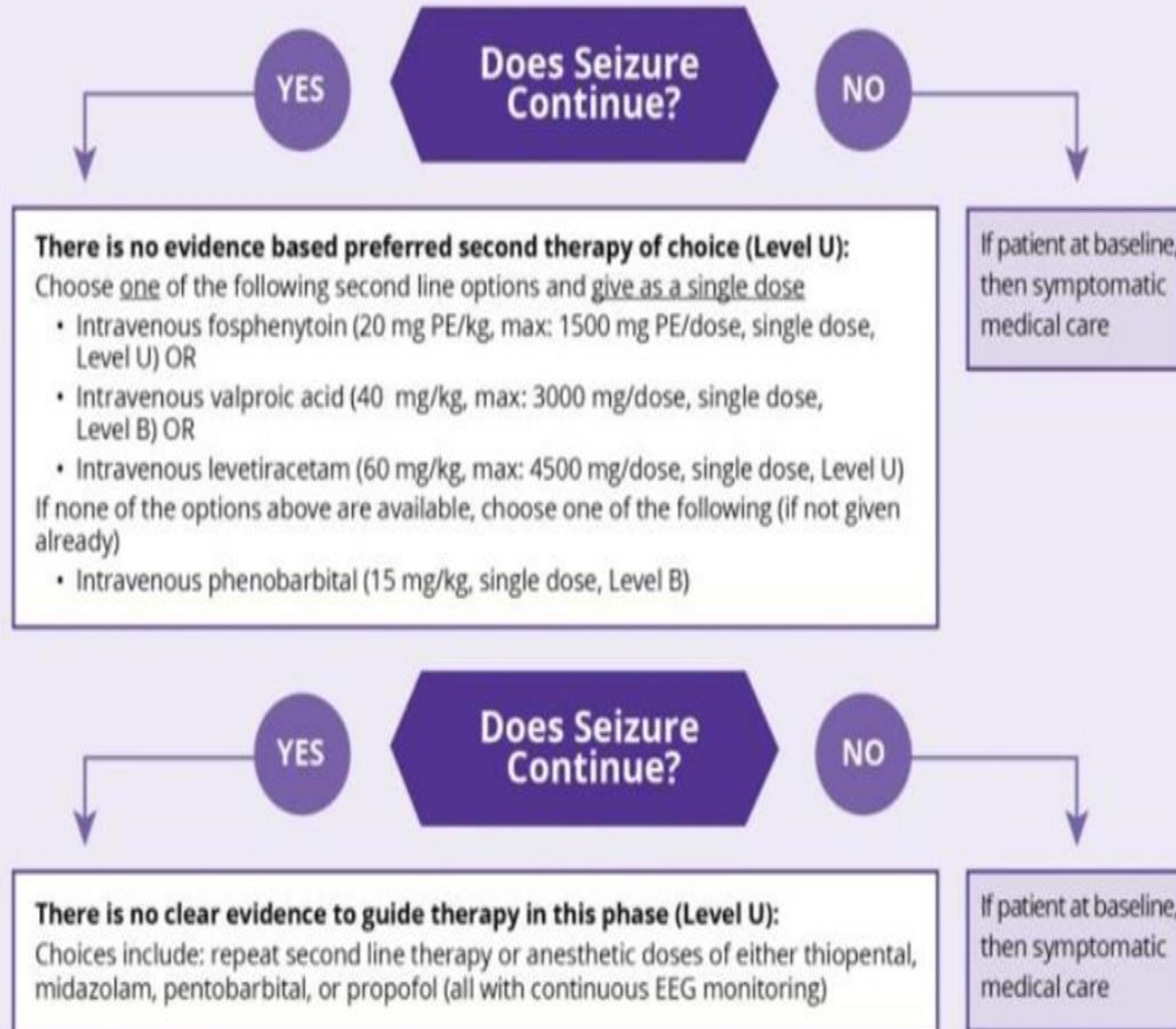
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**5-20 Minutes
Initial Therapy
Phase**



**20-40 Minutes
Second Therapy
Phase**

**40-60 Minutes
Third Therapy
Phase**





Thanks