Epilepsy

Definitions

- ♦ Seizure: the manifestation of an abnormal, hypersynchronous discharge of a population of cortical neurons

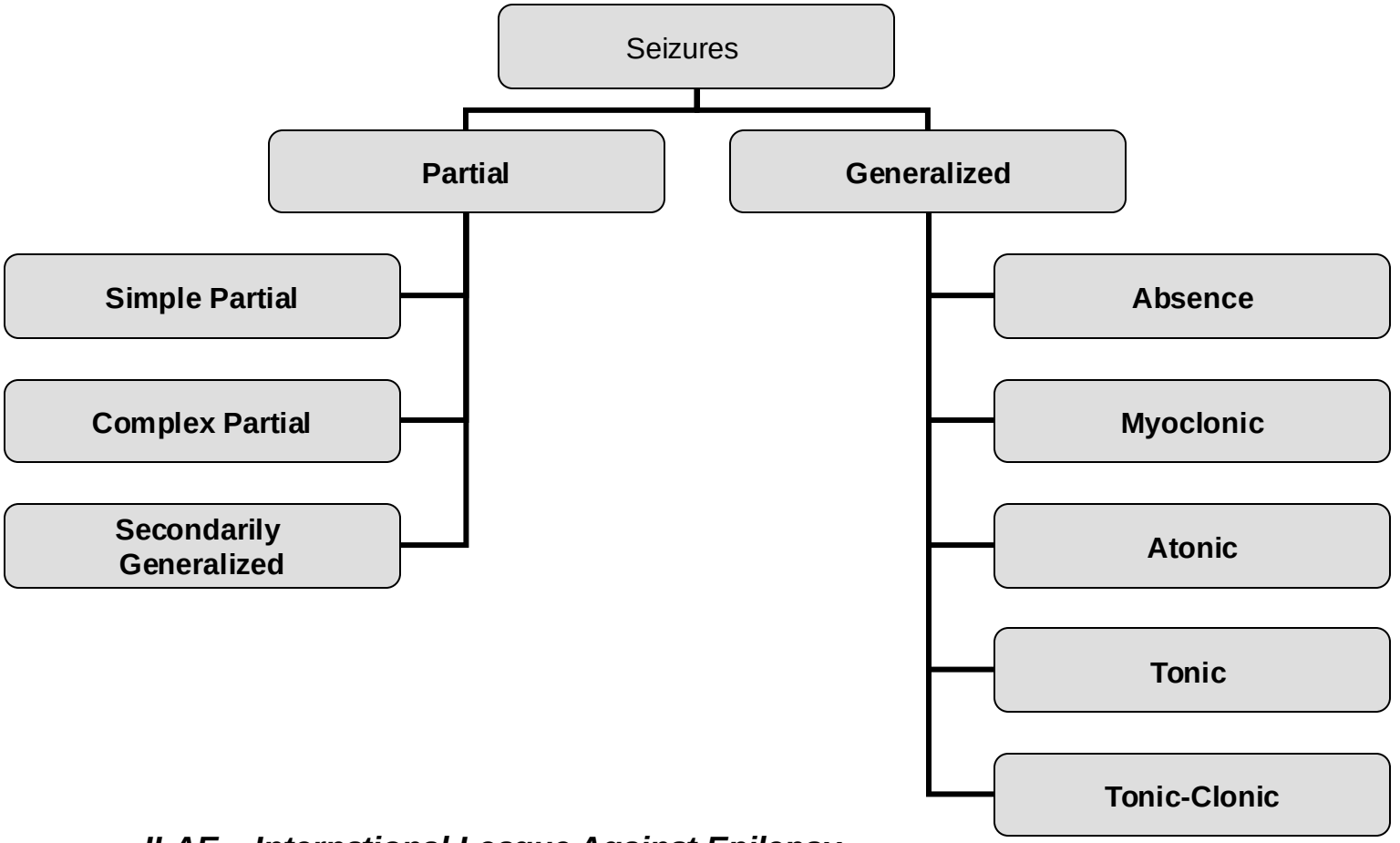
- ♦ Epilepsy: recurrent seizures (two or more) which are not provoked by acute systemic or neurologic insults

Epidemiology of Seizures and Epilepsy

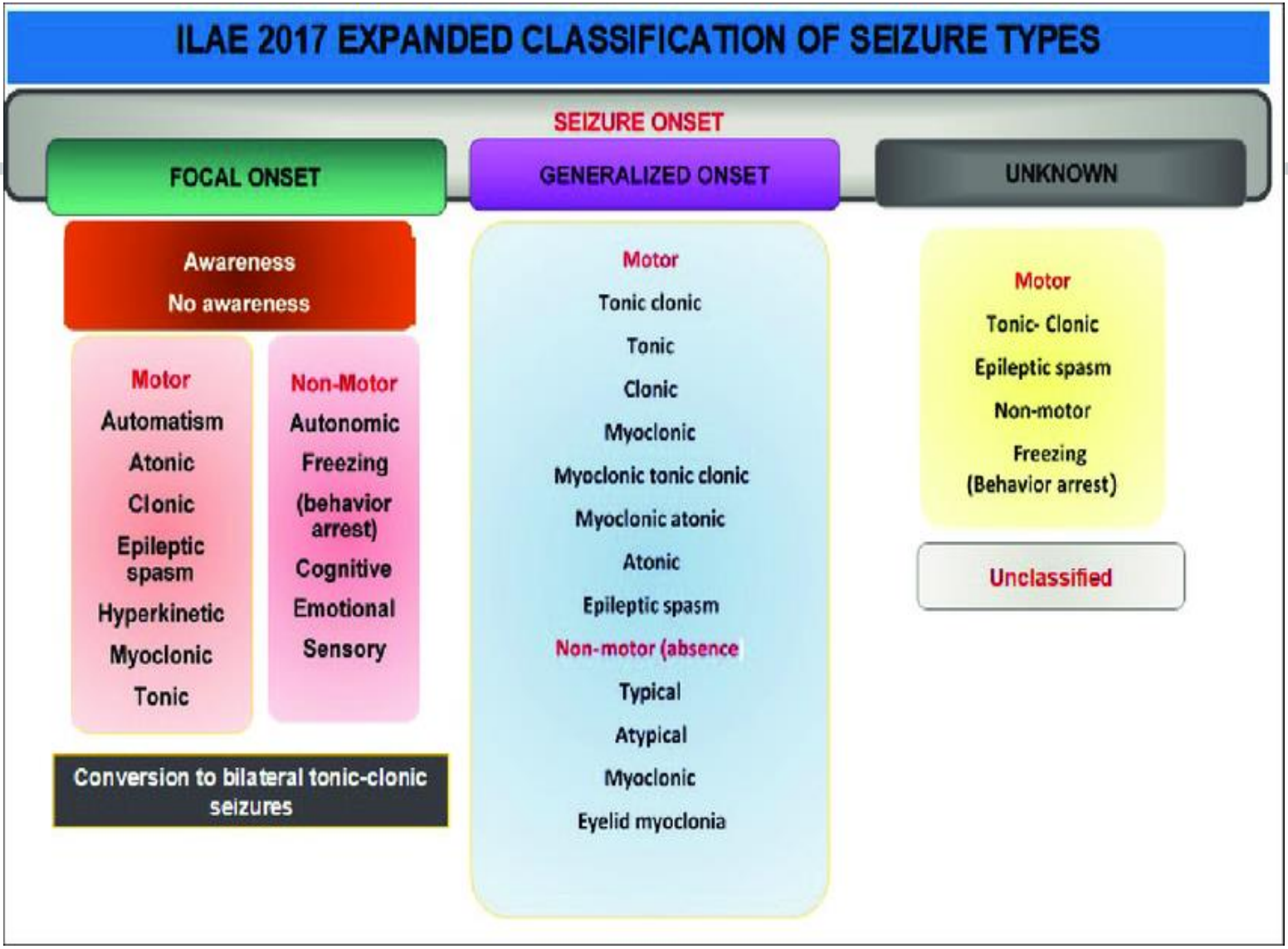
- ♦ Seizures
  - Incidence: 80/100,000 per year
  - Lifetime incidence: 9%
    (1/3 febrile convulsions)

- ♦ Epilepsy
  - Incidence: 45/100,000 per year
  - Point prevalence: 0.5-1%
  - Cumulative lifetime incidence: 3%

ILAE Classification of Seizures



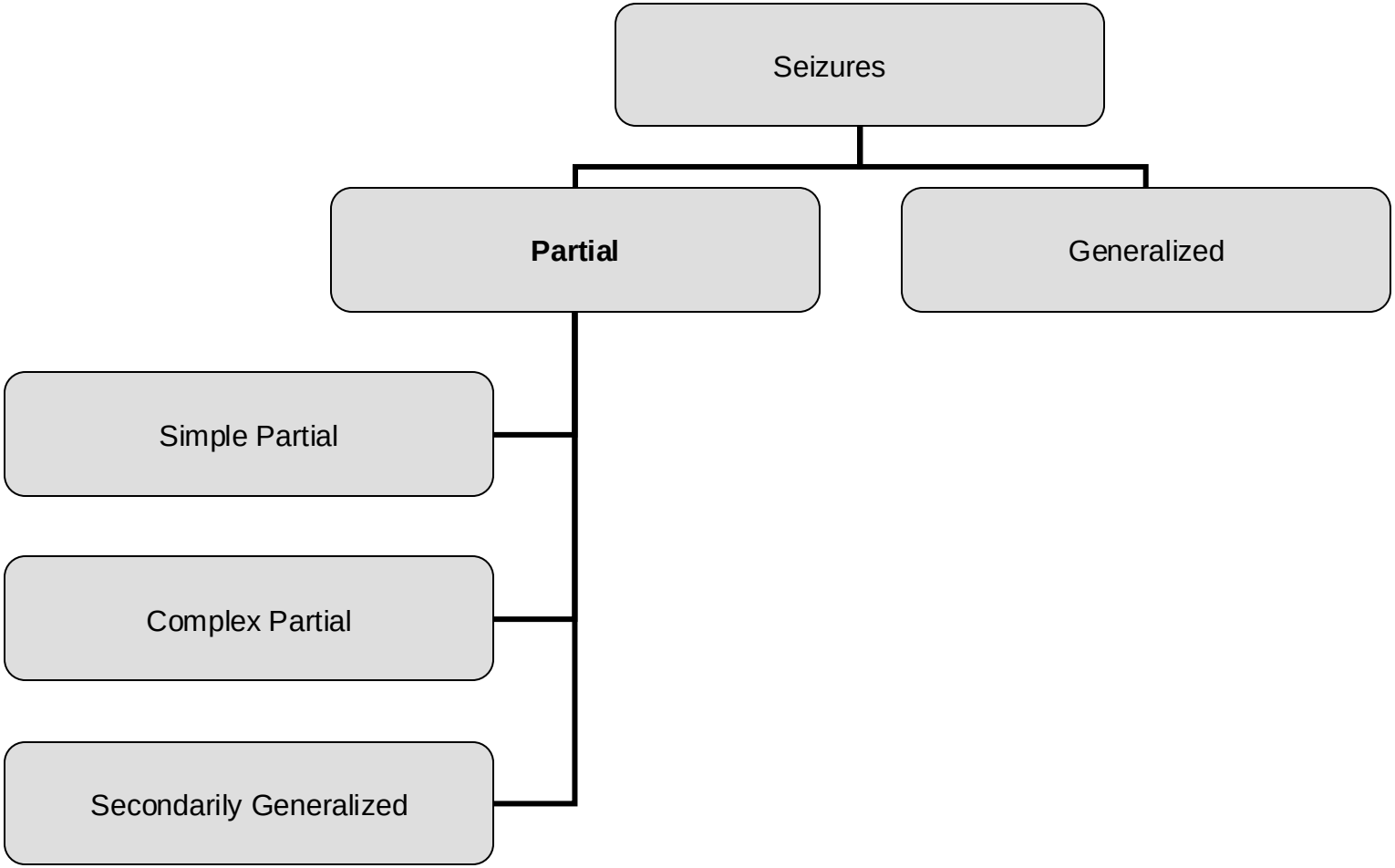
ILAE – International League Against Epilepsy


ILAE 2017 EXPANDED CLASSIFICATION OF SEIZURE TYPES
SEIZURE ONSET
FOCAL ONSET
GENERALIZED ONSET
UNKNOWN
Awareness
No awareness
Motor
Automatism
Atonic
Clonic
Epileptic spasm
Hyperkinetic
Myoclonic
Tonic
Non-Motor
Autonomic
Freezing
(behavior arrest)
Cognitive
Emotional
Sensory
Conversion to bilateral tonic-clonic seizures
Motor
Tonic clonic
Tonic
Clonic
Myoclonic
Myoclonic tonic clonic
Myoclonic atonic
Atonic
Epileptic spasm
Non-motor (absence
Typical
Atypical
Myoclonic
Eyelid myoclonia
Motor
Tonic- Clonic
Epileptic spasm
Non-motor
Freezing
(Behavior arrest)
Unclassified

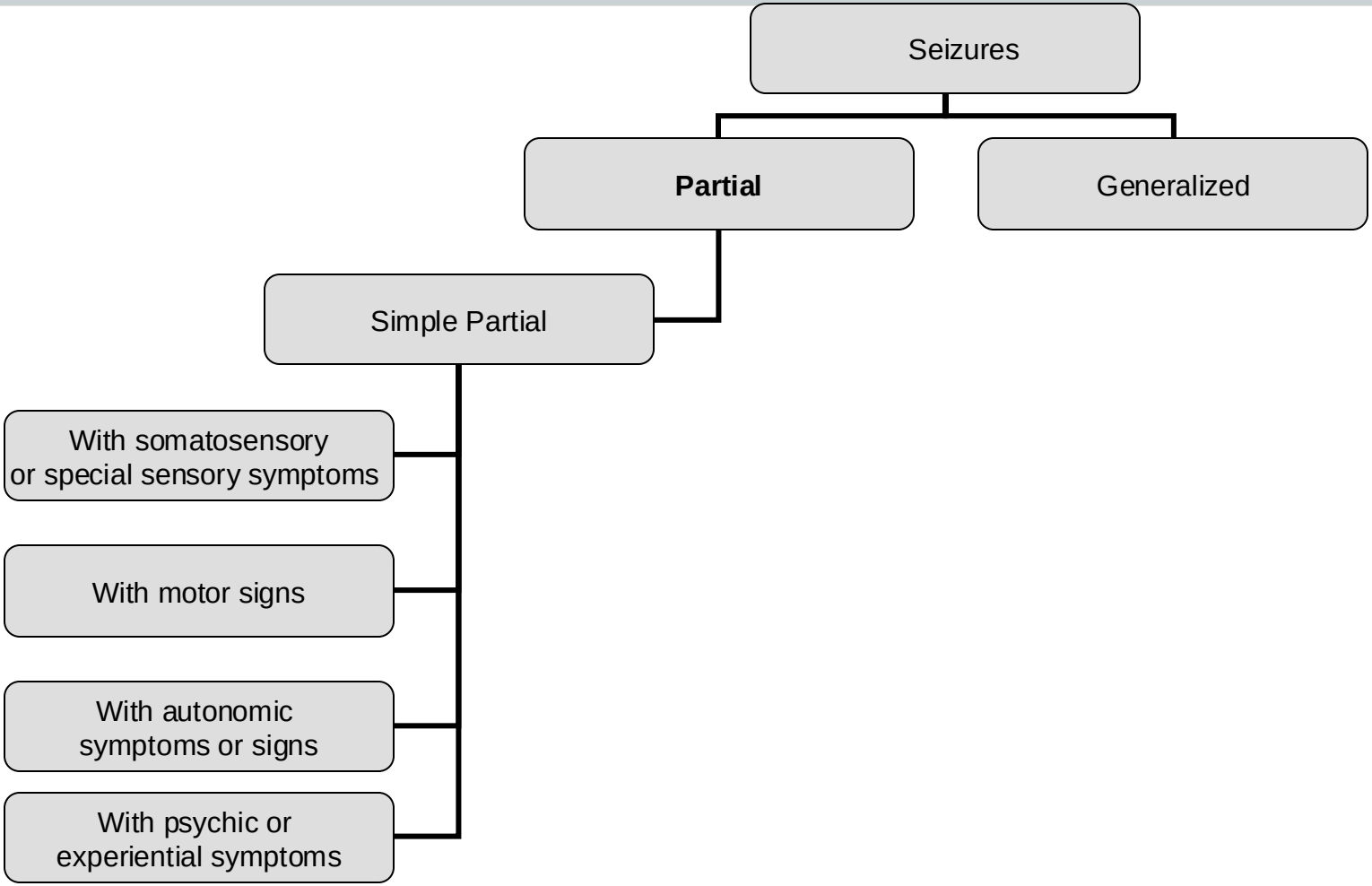
Clinical manifestations of seizures

- The clinical manifestations of a seizure start suddenly and have a short duration (in most cases, lasting between seconds and a few minutes)- transient, self-limited, and paroxysmal
- Attacks are stereotyped
- Not associated with purposeful action.

ILAE Classification of Seizures

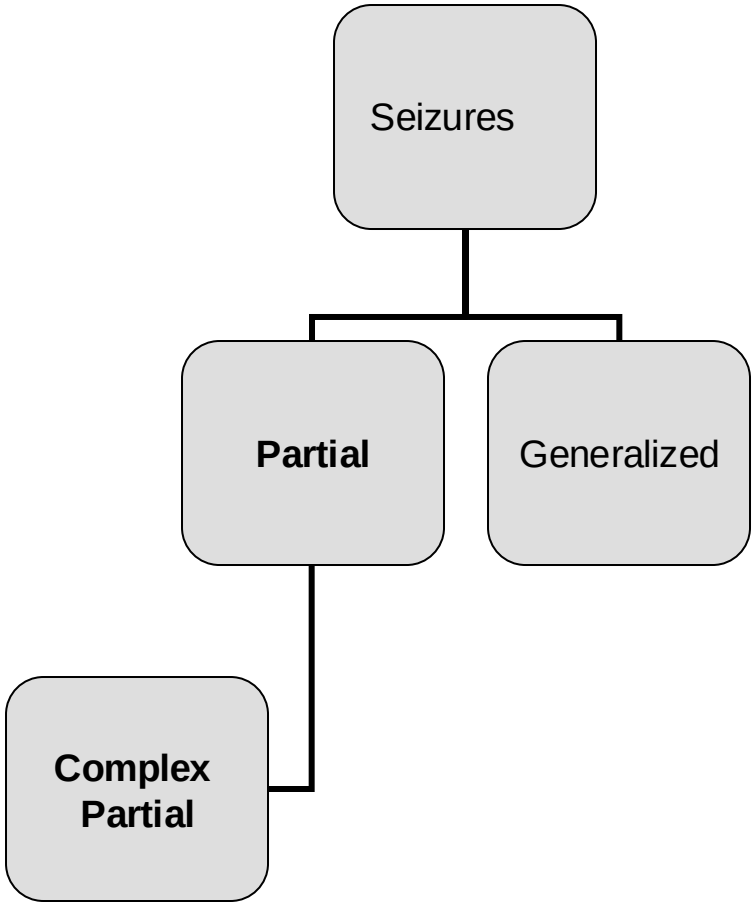


ILAE Classification of Seizures



Complex Partial Seizures

- Impaired consciousness
- Clinical manifestations vary with site of origin and degree of spread
  - Presence and nature of aura
  - Automatisms
  - Other motor activity
- Duration typically < 2 minutes



Typical clinical manifestations of seizures

- Motor (frontal lobe; common): tensing/spasm of whole body or a body part (tonic) or jerking of body (clonic).
- Sensory symptoms (rare) :

  - tingling, vertigo (parietal lobe) ,

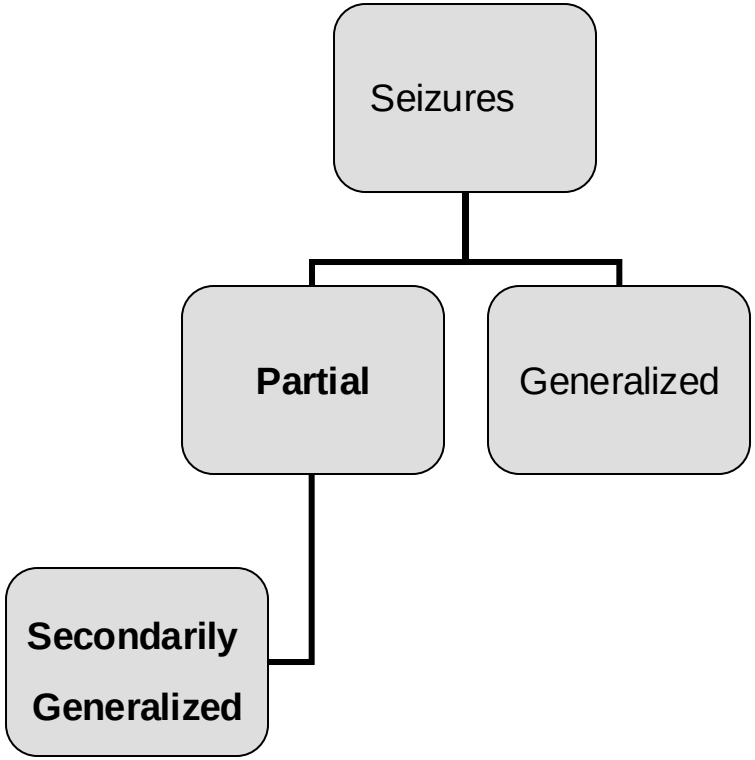
  - visual hallucinations (occipital lobe).

- Psychic/autonomic symptoms (temporal lobe; common): stomach "butterflies", fear, auditory or olfactory hallucinations, deja-vu', jamais-vu', abnormal behavior/talk.

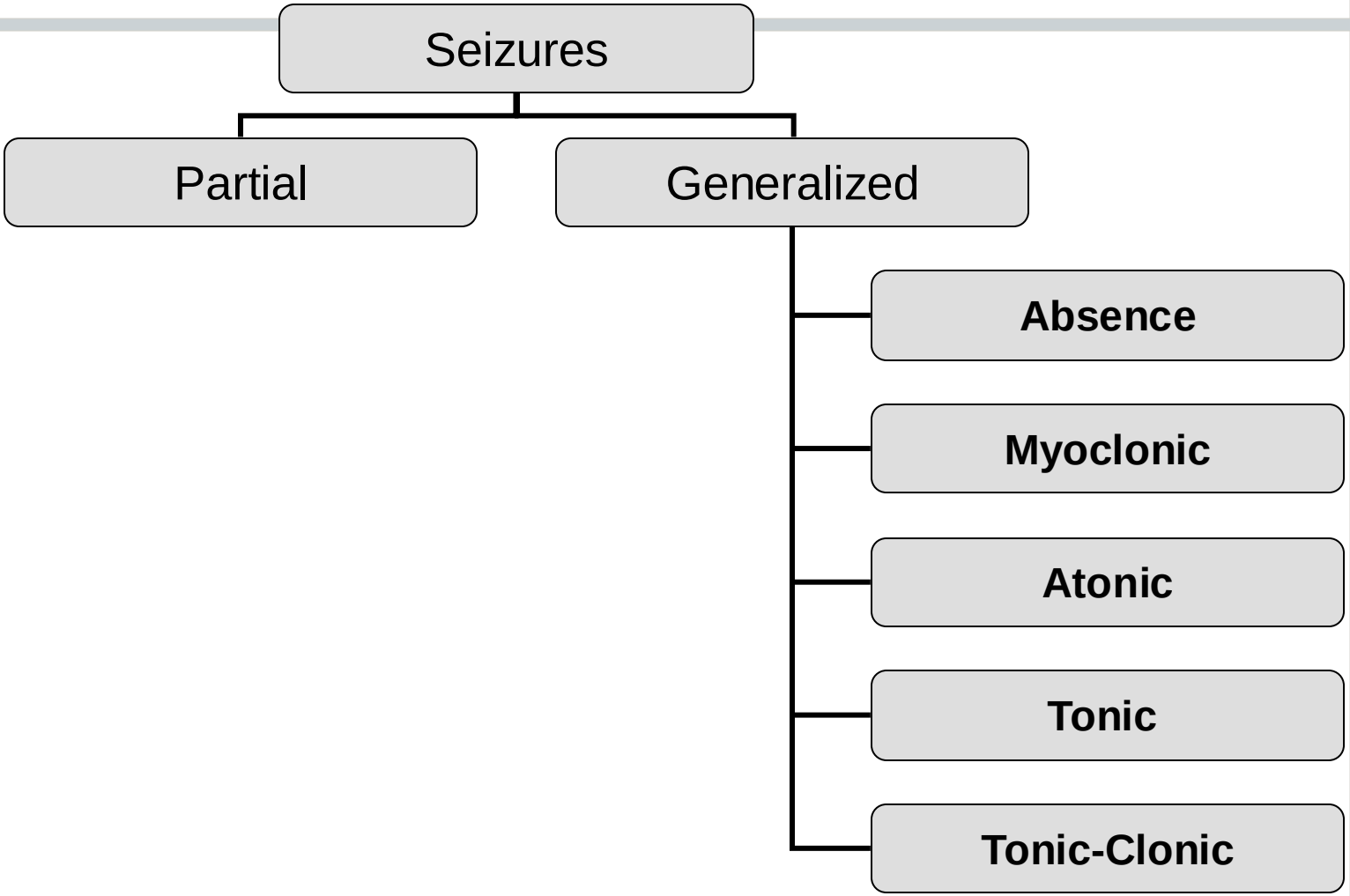
  +/- "automatisms"- oral or hand movements.

Secondarily Generalized Seizures

- Begins focally, with or without focal neurological symptoms
- Variable symmetry, intensity, and duration of tonic (stiffening) and clonic (jerking) phases
- Typical duration 1-3 minutes
- Postictal confusion, somnolence, with or without transient focal deficit

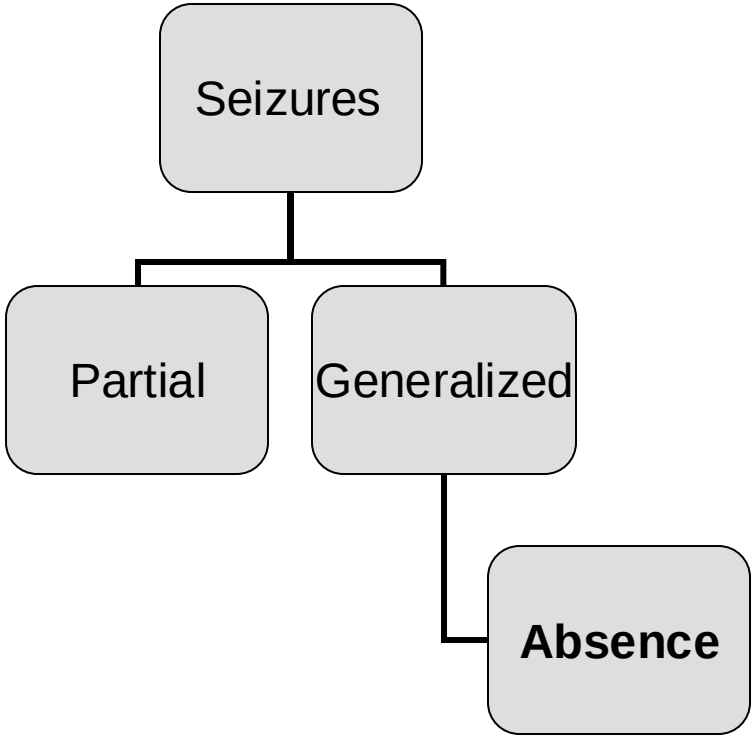


ILAE Classification of Seizures

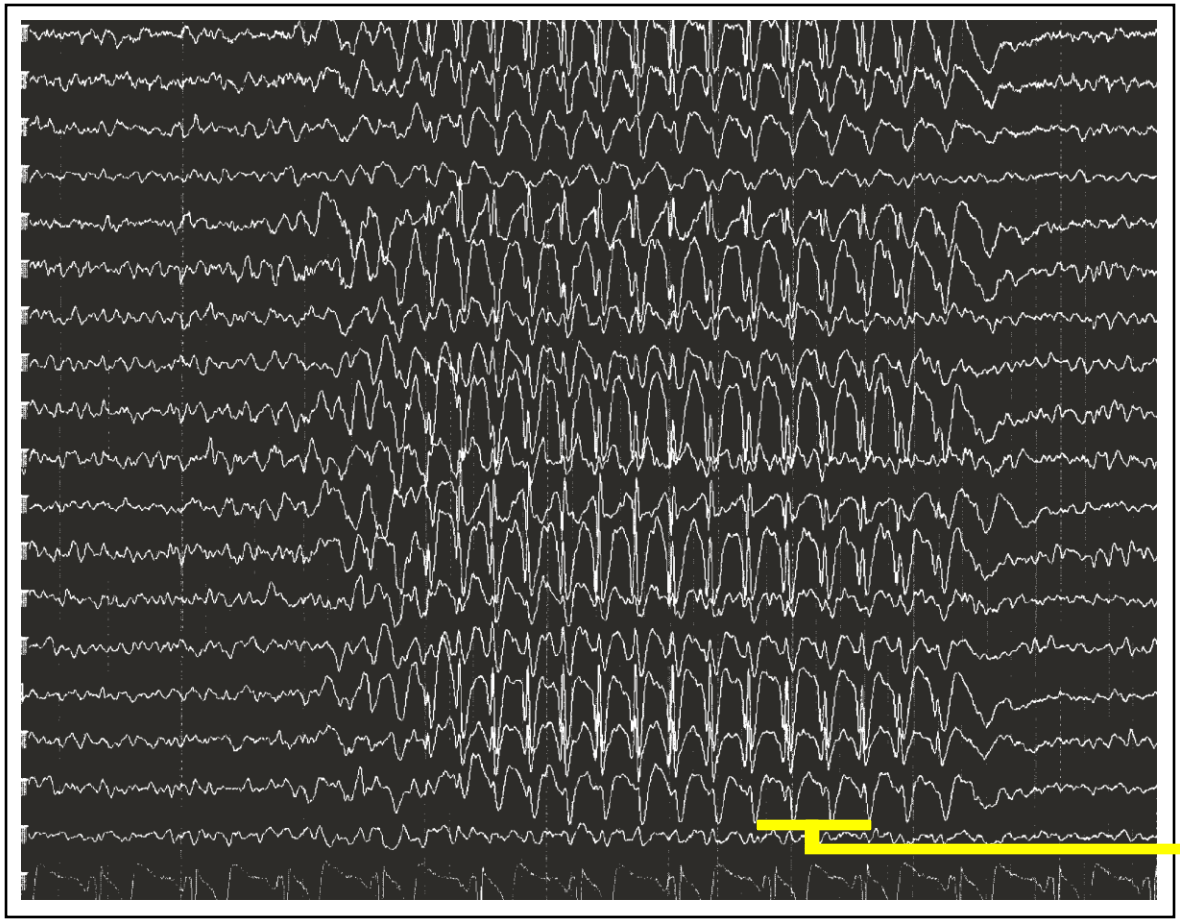


Typical Absence Seizures

- Brief staring spells ("petit mal") with impairment of awareness
  - 3-20 seconds
  - Sudden onset and sudden resolution
  - **Often provoked by hyperventilation**
  - Onset typically between 4 and 14 years of age
  - Often resolve by 18 years of age
- Normal development and intelligence
- EEG: **Generalized 3 Hz spike-wave discharges**



EEG: Typical Absence Seizure



3Hz spike/slow wave complexes

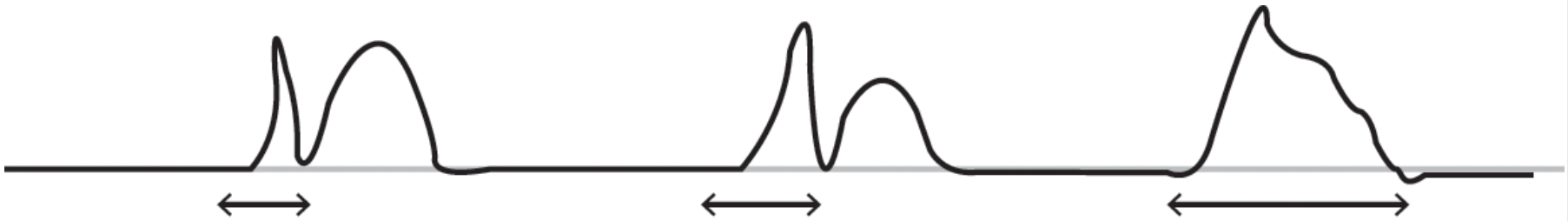
Spike

Slow wave

Spike and wave

Multispike and wave

Epileptiform discharges.



Less than 70 milliseconds

SPIKE WAVE

70–200 milliseconds

SHARP WAVE

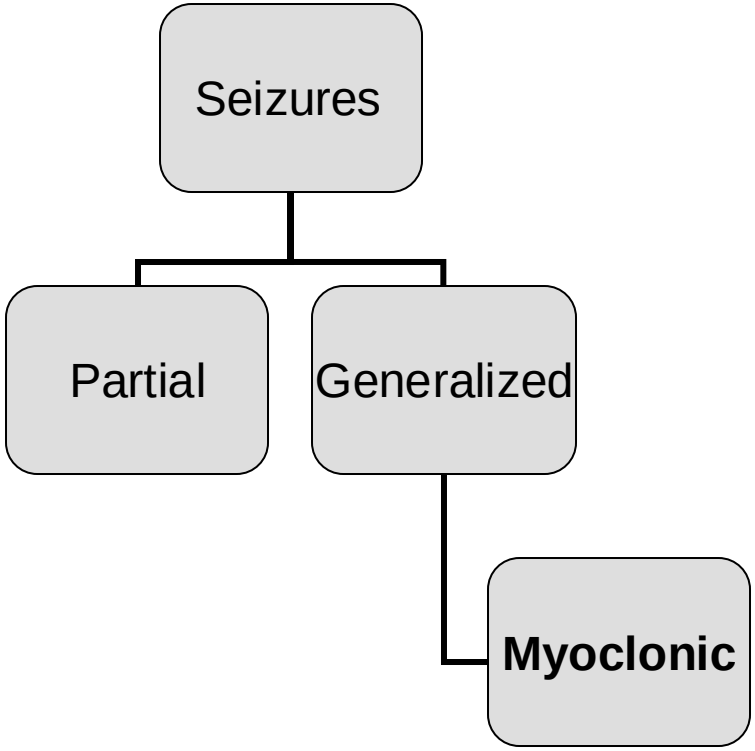
more than 200 milliseconds

SLOW WAVE

Myoclonic Seizures

Epileptic Myoclonus

- Brief, shock-like jerk of a muscle or group of muscles
- Differentiate from benign, nonepileptic myoclonus (e.g., while falling asleep)



Tonic and Atonic Seizures

Tonic seizures

•Symmetric, tonic muscle contraction of extremities with tonic flexion of waist and neck

•Duration - 2-20 seconds.

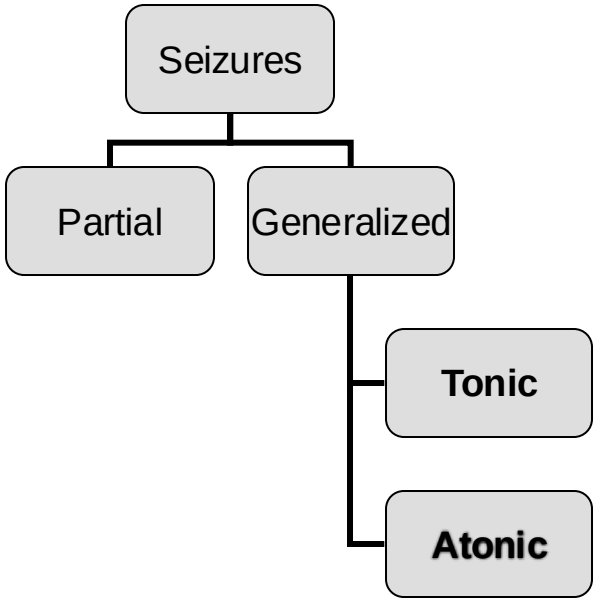
•Atonic seizures

•Sudden loss of postural tone

- When severe often results in falls
- When milder produces head nods or jaw drops.

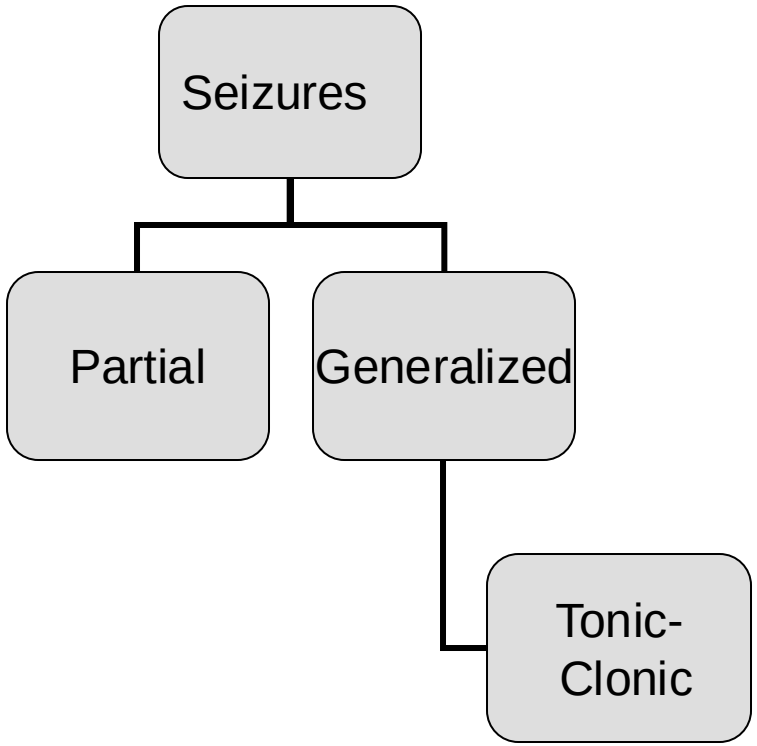
•Consciousness usually impaired

•Duration - usually seconds, rarely more than 1 minute



Generalized Tonic-Clonic Seizures

- Associated with loss of consciousness and post-ictal confusion/lethargy
- Duration 30-120 seconds
- Tonic phase
  - Stiffening and fall
  - Often associated with ictal cry
- Clonic Phase
  - Rhythmic extremity jerking



Etiology of Seizures and Epilepsy

- Infancy and childhood
  - Prenatal or birth injury
  - Inborn error of metabolism
  - Congenital malformation

- Childhood and adolescence
  - Idiopathic/genetic syndrome
  - CNS infection
  - Trauma

Etiology of Seizures and Epilepsy

- Adolescence and young adult
  - Head trauma
  - Drug intoxication and withdrawal*
- Older adult
  - Stroke
  - Brain tumor
  - Acute metabolic disturbances*
  - Neurodegenerative

*causes of acute symptomatic seizures, not epilepsy

Differential Diagnosis of Non-epileptic Events: Physiologic

- Syncope
  - Cardiac (Arrhythmia)
  - Non-Cardiac Syncope (Vasovagal, Dysautonomic)
- Metabolic (Hypoglycemia)
- Migraine
- Sleep Disorders (Narcolepsy)
- Movement Disorders (Paroxysmal Dyskinesia)
- Transient Ischemic Attacks

Differential Diagnosis of Non-epileptic Events: Psychogenic

- Psychogenic Seizures
- Malingering
- Panic Attacks
- Intermittent Explosive Disorder
- Breath-holding Spells

Syncope

- Syncope is transient loss of consciousness due to generalised brain hypoperfusion

- May be cardiac (potentially serious and life-threatening) or reflex/situational syncope (benign)

  - vasovagal

  - cough, micturition, laughing.

  - orthostatic intolerance

Syncope

- Characteristic warning, usually gradual (except with cardiac arrhythmia)
- Typical precipitants (except with cardiac arrhythmia)
- Minimal to no postictal confusion/somnolence
- Convulsive syncope — tonic>clonic manifestations, usually < 30 sec

Reflex Syncope

- Most transient loss of consciousness is reflex (vasovagal) syncope, attributable to an overactive autonomic nervous system in a young healthy person.
- The classical tetrad (four Ps) of:
- posture (onset when upright),
- prodrome (blurring or blacking of vision, nausea, light headedness and sweating),
- provoking factors (sight of blood, pain and bathroom) and
- prompt recovery

are helpful pointers, though none is diagnostic alone.

Syncope vs Seizure: Before Spell

	Syncope	**Seizure**
Trigger (position, emotion, Valsalva)	Common	Rare
Sweating & nausea	Common	Rare
Aura (e.g. déjà vu, smell) or unilateral symptoms	Rare	Common

Syncope vs Seizure: During Spell

	Syncope	**Seizure**
Pallor	Common	Rare
Cyanosis	Rare	Common
Loss of consciousness	<20 secs	>60 secs

Syncope vs Seizure: During Spell

	Syncope	**Seizure**
Automatisms	Occasional	Common
Tongue biting, lateral	Rare	Occasional
Frothing/hyper-salivation	Rare	Common

- Lateral tongue biting is poorly sensitive but highly specific (99%) for a generalized seizure.
- Lateral tongue biting usually indicates true epileptic seizures as opposed to bites to the tip of the tongue which are typically non-epileptiform events.

Syncope vs Seizure: During Spell

	Syncope	**Seizure**
Movements	Few clonic or myoclonic jerks or brief tonic posturing	Prolonged tonic phase » rhythmic clonic mvmts
Duration	< 15 seconds	30 -120 seconds
Frothing/hyper-salivation	Rare	Common

Syncope vs Seizure: After spell

	Syncope	**Seizure**
Confusion/ disorientation	Rare; <30 secs	Common; several mins or longer
Diffuse myalgias	Rare, brief, usually shoulders/chest	Common, hours-days
Creatine kinase elevation	Rare	Common

Features That Are Not Helpful in Differentiating Syncope from Seizure

- Incontinence
- Prolactin level
- Dizziness
- Fear
- Injury other than lateral tongue biting
- Eye movements (rolling back)
- Brief automatisms

Migraine aura vs. occipital seizure

	Migraine	**Occipital Seizure**
Duration	5-20 min	0.5-5 min
Typical Content	B&W; straight lines; slow spread	Color, round, variable spread
Laterality	Either side	Always same side (contralateral)
Associated Features		Altered awareness, automatisms

Psychogenic Non-epileptic Seizures

- 10-45% of patients referred for intractable spells
- Females > males
- Psychiatric mechanism — dissociation, conversion
- Common association with physical, emotional, or sexual abuse

Once recognized, approximately 50% respond well to specific psychiatric treatment

Epileptic and nonepileptic seizures may co-exist

Video-EEG monitoring often required for diagnosis

Psychogenic Non-epileptic Seizures

FEATURES SUGGESTIVE OF NONEPILEPTIC PSYCHOGENIC SEIZURES

- Eye Closure
- Pelvic thrusting
- Opisthotonus
- Side-to-side head shaking
- Prolonged duration (>4 minutes)
- Stopping and starting
- Suggestibility

Psychogenic Non-epileptic Seizures

Features suggestive of Non-epileptic seizures	**Important Caveats**
Thrashing, struggling, crying, pelvic thrusting, side-to-side rolling, wild movements	Bizarre complex automatisms can occur with frontal lobe seizures
Preserved consciousness with bilateral tonic or clonic mts	Frontal lobe seizures may have bilateral convulsive movements without impairment of consciousness
Lack of postictal confusion	Posti-ictal confusion is often absent after frontal lobe seizures
Postictal crying or shouting	Aggressive and emotional behavior can occur after epileptic seizures

Clinical distinction of dissociative non-epileptic attacks ("pseudoseizures") from epileptic seizures

	Dissociative non-epileptic seizures ("pseudoseizures")	Epileptic seizures
Induced by anger, panic, suggestion	Common	Rare
Onset	Often gradual	Usually sudden
Duration	Often prolonged, occasionally hours	1–3 minutes
Breathing and colour	Breathing continues, stays pink	Usually apnoeic and cyanosed
Retained consciousness	Common	Uncommon
Pelvic thrusting, back arching, erratic movements	Common	Rare
Fighting, held down, may injure others	Common	Rare
Eyes closed	Common	Less common
Resisting eye opening and eye contact	Common	Rare
Occur only in company	Common	Rare
Lateral tongue bite	Rare (minor)	Common
Self injury	Rare	Common (occasionally serious)
Incontinence	Rare (occasionally with experience)	Common
Post-ictal confusion	Rare	Common

Back arching in PNES

Diagnosis

- Epilepsy is a clinical diagnosis– patients present with recurrent stereotyped attacks of one or more of the previous clinical manifestations.
- Exclude mimics….ECG before EEG
- Blood tests/ toxicology screen
- Brain imaging (CT,MRI)
- Electroencephalogram (EEG).

First Aid
Tonic-Clonic Seizure

- After seizure ends, turn person on side with face turned toward ground to keep airway clear, protect from nearby hazards
- Transfer to hospital needed for:
  - Multiple seizures or status epilepticus
  - Person is pregnant, injured, diabetic
  - New onset seizures
- DO NOT put any object in mouth or restrain

Evaluation of a First Seizure
Exclude provoking factors

- History, physical
- Blood tests: CBC, electrolytes, glucose, calcium, magnesium, phosphate, hepatic and renal function
- Lumbar puncture
  (only if meningitis or encephalitis suspected and potential for brain herniation is excluded)
- Blood or urine screen for drugs
- Electroencephalogram (EEG)
- CT or MR brain scan
- Start AED if 2 or more unprovoked seizures or one seizure with high likelihood of recurrence

Seizure Precipitants

- Metabolic and Electrolyte Imbalance
- Stimulant/other proconvulsant intoxication
- Sedative or ethanol withdrawal
- Sleep deprivation
- Antiepileptic medication reduction or inadequate AED treatment
- Hormonal variations
- Stress
- Fever or systemic infection
- Concussion and/or closed head injury

Seizure Precipitants (cont.)

Metabolic and Electrolyte Imbalance

- Low blood glucose
  (or high glucose, esp. w/ hyperosmolar state)
- Low sodium
- Low calcium
- Low magnesium

AED Choice: Attempt Monotherapy

- Simplifies treatment
- Reduces adverse effects
- Conversion to monotherapy
  - Eliminate sedative drugs first
  - Withdraw antiepileptic drugs slowly over several months

AED Choice: More Considerations

- Limited placebo-controlled trials available, particularly of newer AEDs
- Several drugs are commonly used for indications other than those for which they are officially approved/recommended
- Choice of AED for **partial epilepsy**:
  - drug side-effect profile and patient's preference/concerns
- Choice of AED for **generalized epilepsy**:
  - predominant seizure type(s)
  - drug side-effect profile and patient's preference/concerns

See appendix for

ILAE Summary Guidelines and Summary of AAN evidence-based guidelines

AED Mechanisms of Action

AED	Na^+ Channel Blockade	Ca^{++} Channel Blockade	H-current enhance-ment	Glutamate Receptor Antagonism	GABA Enhance-ment	Carbonic Anhydrase Inhibition
PHT	X			X (NMDA glycine)		
CBZ, OXC	X				X (CBZ>OXC)	
barb, benzo					X ($GABA_A$)	
ESM		X				
VPA	X	X			X	
FBM	X	X		X (NMDA)	X	
GBP		X	X	X (NMDA glycine)		
LTG	X		X	X (kainate)		
TPM	X	X		X (AMPA,kainate)	X	X
TGB					X (reuptake)	
LEV				X (kainate)		
ZNS	X	X				X
PGB		X				
LCM	X (slow inact.)					
RUF	X					
VGB					X (metab.)	

Modified from White HS and Rho JM, Mechanisms of Action of AEDs, 2010.

AEDs: Common Adverse Effects

Typically dose-related:

Dizziness , Fatigue , Ataxia, Diplopia
- all AEDs

Irritability, neuropsychiatric side effects
- Levetiracetam, ezogabine

Word-finding difficulty
- Topiramate

Weight loss/anorexia
- Topiramate, zonisamide, felbamate

Weight gain
- Valproate (also associated with polycystic ovarian syndrome)
- Carbamazepine, gabapentin, pregabalin

AEDs: Serious Adverse Effects

Typically Idiosyncratic:

Renal stones
- Topiramate, zonisamide

Anhydrosis, heat stroke
- Topiramate, Zonisamide

Acute closed-angle glaucoma
- Topiramate

Hyponatremia
- Carbamazepine, oxcarbazepine

Urinary Retention
- Ezogabine

AEDs: Serious Adverse Effects

Typically Idiosyncratic:

Aplastic anemia
- Felbamate, zonisamide, valproate, carbamazepine

Hepatic Failure
- Valproate, felbamate, lamotrigine, phenobarbital

Peripheral vision loss
- Vigabatrin

Rash
- Phenytoin, lamotrigine, zonisamide, carbamazepine

Stevens-Johnson Syndrome (SJS) / Toxic Epidermal Necrolysis (TENS)

- Severe life threatening allergic reaction
- Blisters and erosions of the skin, particularly palms/soles and mucous membranes
- Fever and malaise
- Rare: severe risk roughly 1-10/10,000 for many AEDs
  - *Rapid titration of lamotrigine especially in combination with valproate increases risk*

Psychosocial Concerns and Quality of Life in Epilepsy

- The most common concerns noted by patients with epilepsy:
  - Driving (70%)
  - Independence
  - Work and Education
  - Social Embarrassment
  - Medication Dependence
  - Mood/Stress
  - Safety

Status Epilepticus

- Definition
  - More than 5 minutes of continuous clinical or electrographic seizure activity

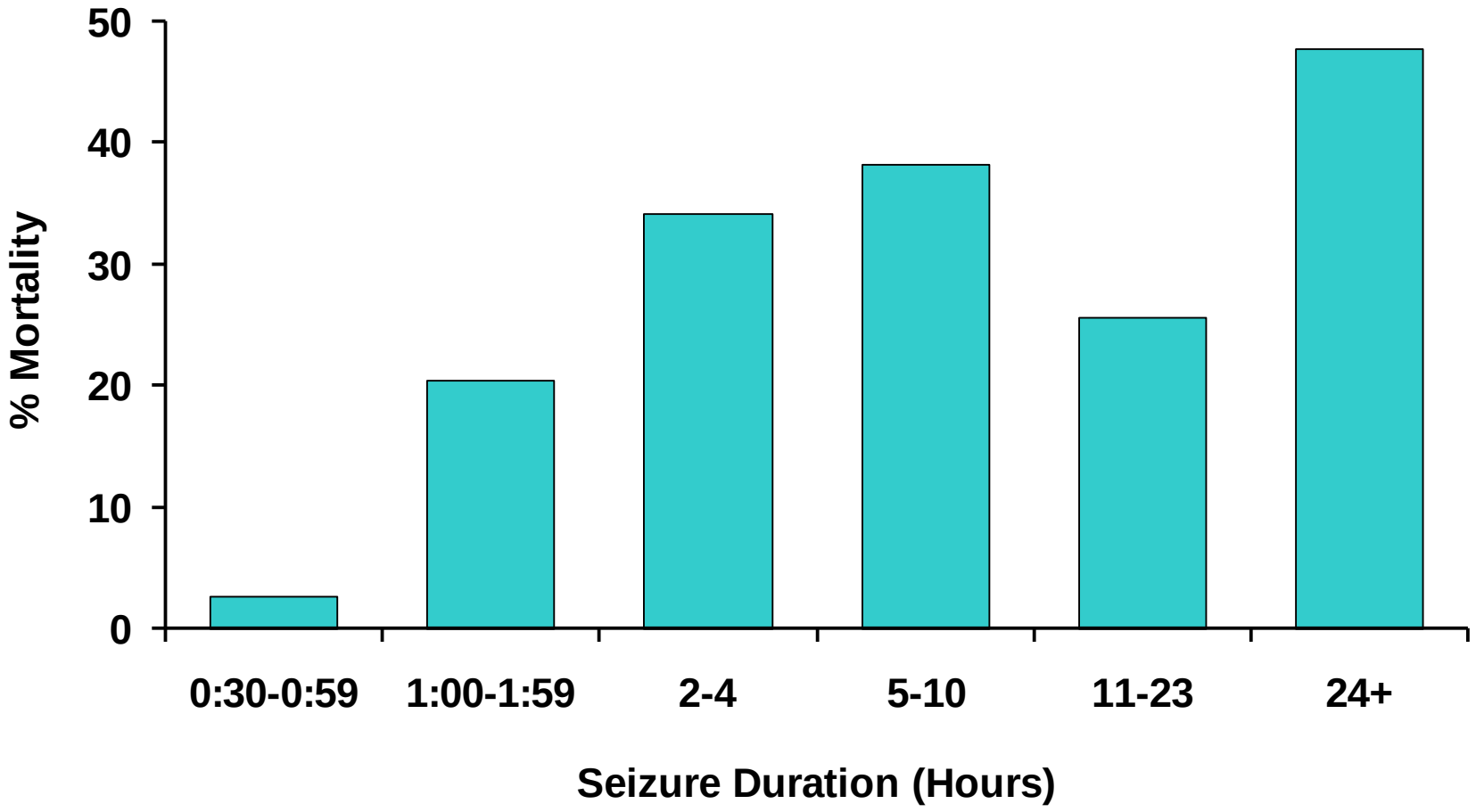
    or

  - Two or more sequential seizures without full recovery between seizures

Status Epilepticus (SE)

- A medical emergency
  - Adverse consequences can include hypoxia, hypotension, acidosis, hyperthermia, rhabdomyolysis and neuronal injury
  - Know the recommended sequential protocol for treatment and distribute a written protocol to emergency rooms, ICUs and housestaff.
  - Goal: stop seizures as soon as possible

Mortality of SE by duration



SE Treatment Algorithm

- Check emergency ABC's
- Give O2
- Obtain IV access
- Begin EKG monitoring
- Check fingerstick glucose
- Draw blood for Chem-7, Magnesium, Calcium, Phosphate, CBC, LFTs, AED levels, ABG, troponin
- Toxicology screen (urine and blood).
- Thiamine 100 mg IV; 50 ml of D50 IV unless adequate glucose known.

Status Epilepticus: First-line Treatment Options

Benzodiazepine	Route	Dosing	Maximum Dose	Class & Level of Evidence
LORAZEPAM	IV	0.1mg/kg	4mg @ 2mg/min May repeat x1 in 5-10 min	Class I Level A
MIDAZOLAM	IM Nasal Buccal	0.2mg/kg	10mg	Class I Level A
DIAZEPAM	PR	0.2mg/kg	20mg	Class IIa, Level A

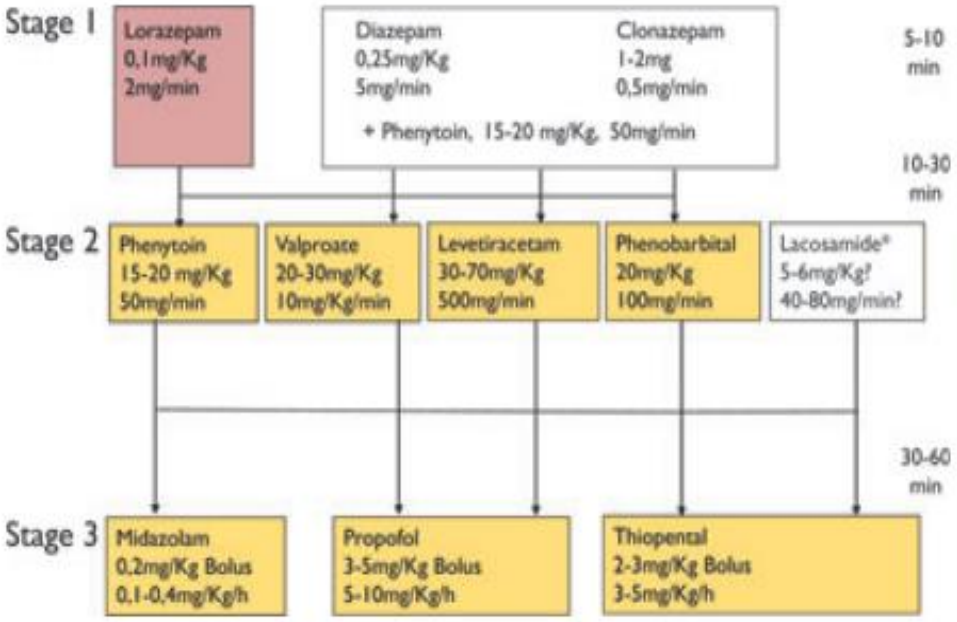


Figure 5.

Staged approach to the treatment of convulsive status epilepticus. *There is currently limited evidence for the use of lacosamide in SE (see Höfler et al., 2011) Modified after Trinka, 2007; Shorvon et al., 2008.

Epilepsia © ILAE

- Register your attendance with your university number
- Make sure that the settings of your phone allow tracking location

Go to settings > privacy> location> services> make sure that location services is ON