

# Epilepsy

# Definitions

- ♦ Seizure: the manifestation of an abnormal, hypersynchronous discharge of a population of cortical neurons
- ♦ Epilepsy: A disorder where there is tendency to have recurrent seizures (two or more not within 24 hours) 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 2017 EXPANDED CLASSIFICATION OF SEIZURE TYPES

## SEIZURE ONSET

### FOCAL ONSET

#### 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

### GENERALIZED ONSET

#### Motor

Tonic clonic  
Tonic  
Clonic  
Myoclonic  
Myoclonic tonic clonic  
Myoclonic atonic  
Atonic  
Epileptic spasm

#### Non-motor (absence)

Typical  
Atypical  
Myoclonic  
Eyelid myoclonia

### UNKNOWN

#### 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.**

# Common clinical manifestations of focal 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.

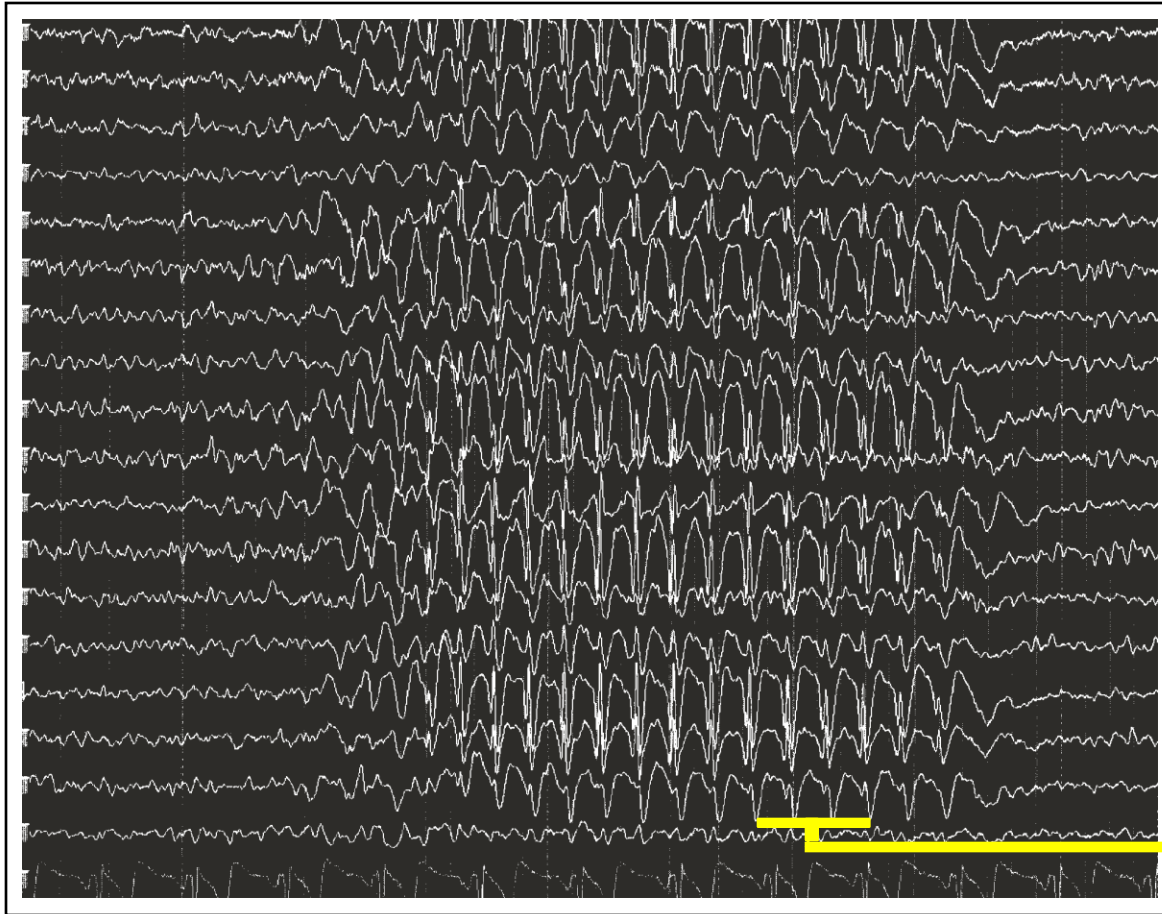
# Secondarily Generalized Seizures

- ♦ 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

# 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**
- Treatment: Ethosuximide , Lamotrigine , Sodium Valproate

# EEG: Typical Absence Seizure



**3Hz  
spike/slow  
wave  
complexes**

# 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

# 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<br>(position, emotion, Valsalva)             | Common  | Rare    |
| Sweating & nausea                                    | Common  | Rare    |
| Aura (e.g. déjà vu, smell)<br>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**

|                           | <b>Syncope</b> | <b>Seizure</b> |
|---------------------------|----------------|----------------|
| Automatisms               | Occasional     | Common         |
| Tongue biting, lateral    | Rare           | Occasional     |
| Frothing/hyper-salivation | Rare           | Common         |

# 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/<br>disorientation | Rare; <30 secs                          | Common;<br>several mins or<br>longer |
| Diffuse myalgias             | Rare, brief, usually<br>shoulders/chest | Common,<br>hours-days                |
| Creatine kinase<br>elevation | 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.



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# Migraine aura vs. occipital seizure

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

| <b>Features suggestive of Non-epileptic seizures</b>                                  | <b>Important Caveats</b>                                                                          |
|---------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| 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<br>("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                        |

# 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 **focal 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 <sup>+</sup><br>Channel<br>Blockade | Ca <sup>++</sup><br>Channel<br>Blockade | H-current<br>enhance-<br>ment | Glutamate<br>Receptor<br>Antagonism | GABA<br>Enhance-<br>ment | Carbonic<br>Anhydrase<br>Inhibition |
|-------------|----------------------------------------|-----------------------------------------|-------------------------------|-------------------------------------|--------------------------|-------------------------------------|
| PHT         | X                                      |                                         |                               | X (NMDA glycine)                    |                          |                                     |
| CBZ, OXC    | X                                      |                                         |                               |                                     | X (CBZ>OXC)              |                                     |
| barb, benzo |                                        |                                         |                               |                                     | X (GABA <sub>A</sub> )   |                                     |
| 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)

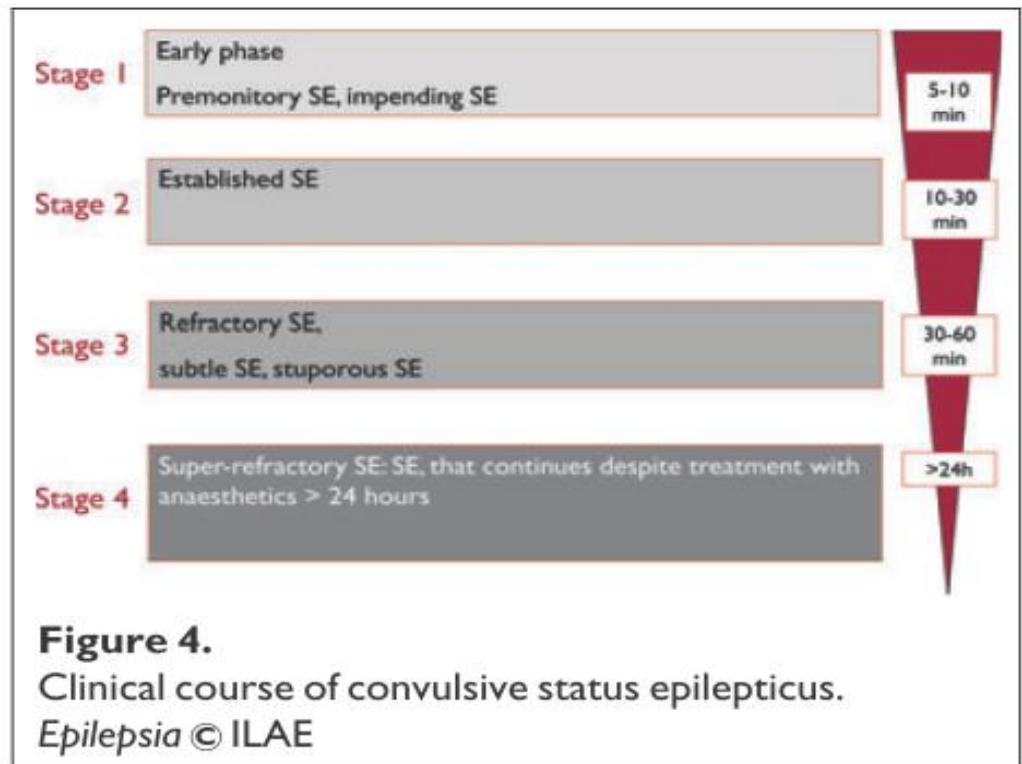
- ♦ Severe life threatening allergic reaction
- ♦ Blisters and erosions of the skin, particularly palms/soles and mucous membranes
- ♦ Fever and malaise
- ♦ Rare: severe risk roughly 1-10/10,000 for many AEDs
  - ♦ *Rapid titration of lamotrigine especially in combination with valproate increases risk*

# 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

If the patient has a prolonged ( $>5$  min.) seizure or repetitive (3 or more/hr) seizures without recovery between episodes, they are considered to be in SE and the Rx protocol initiated.



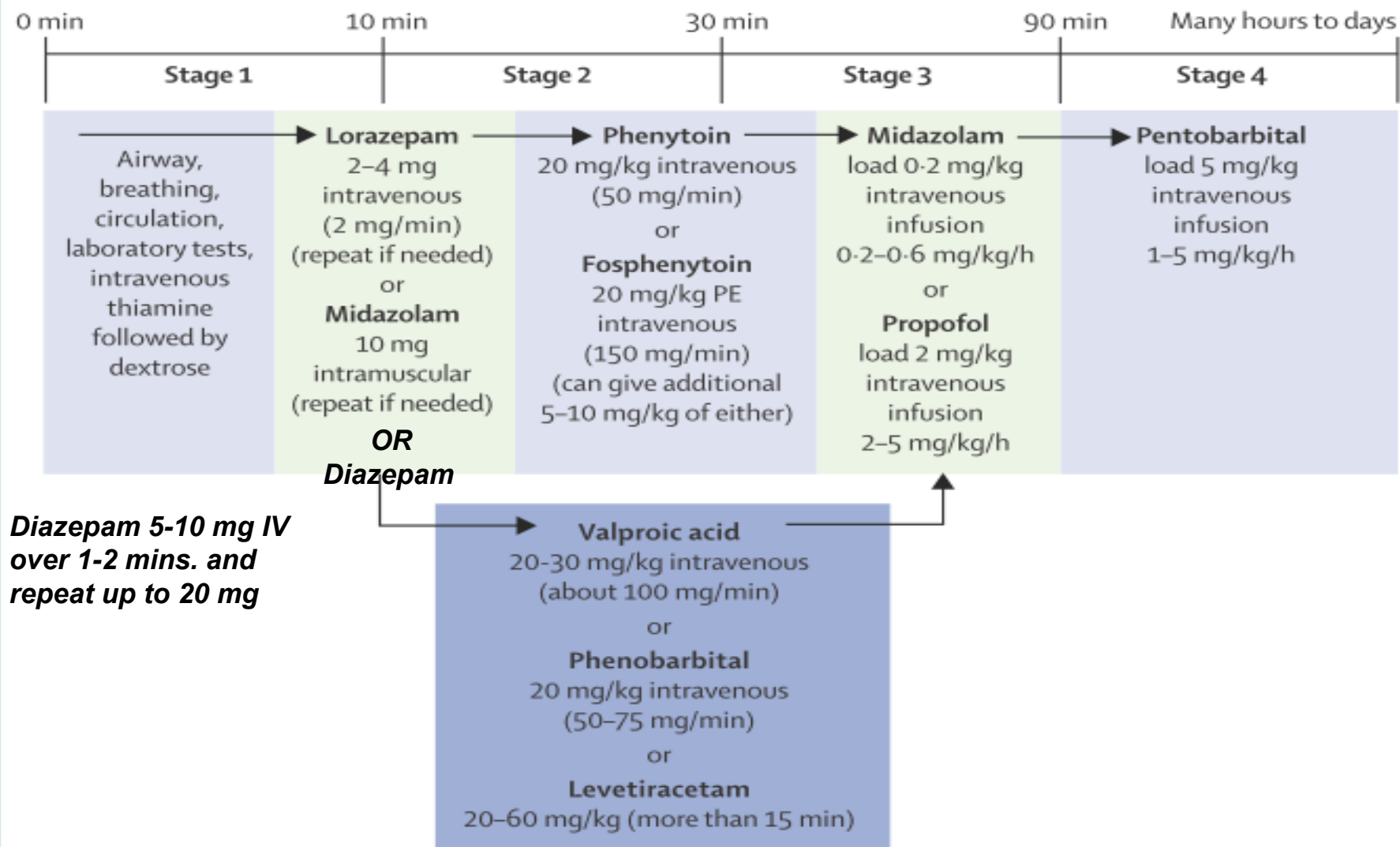
# Status Epilepticus (SE)

- ♦ A medical emergency
  - Adverse consequences can include hypoxia, hypotension, acidosis, hyperthermia, rhabdomyolysis and neuronal injury
  - Goal: stop seizures as soon as possible and treat the underlying cause if possible.

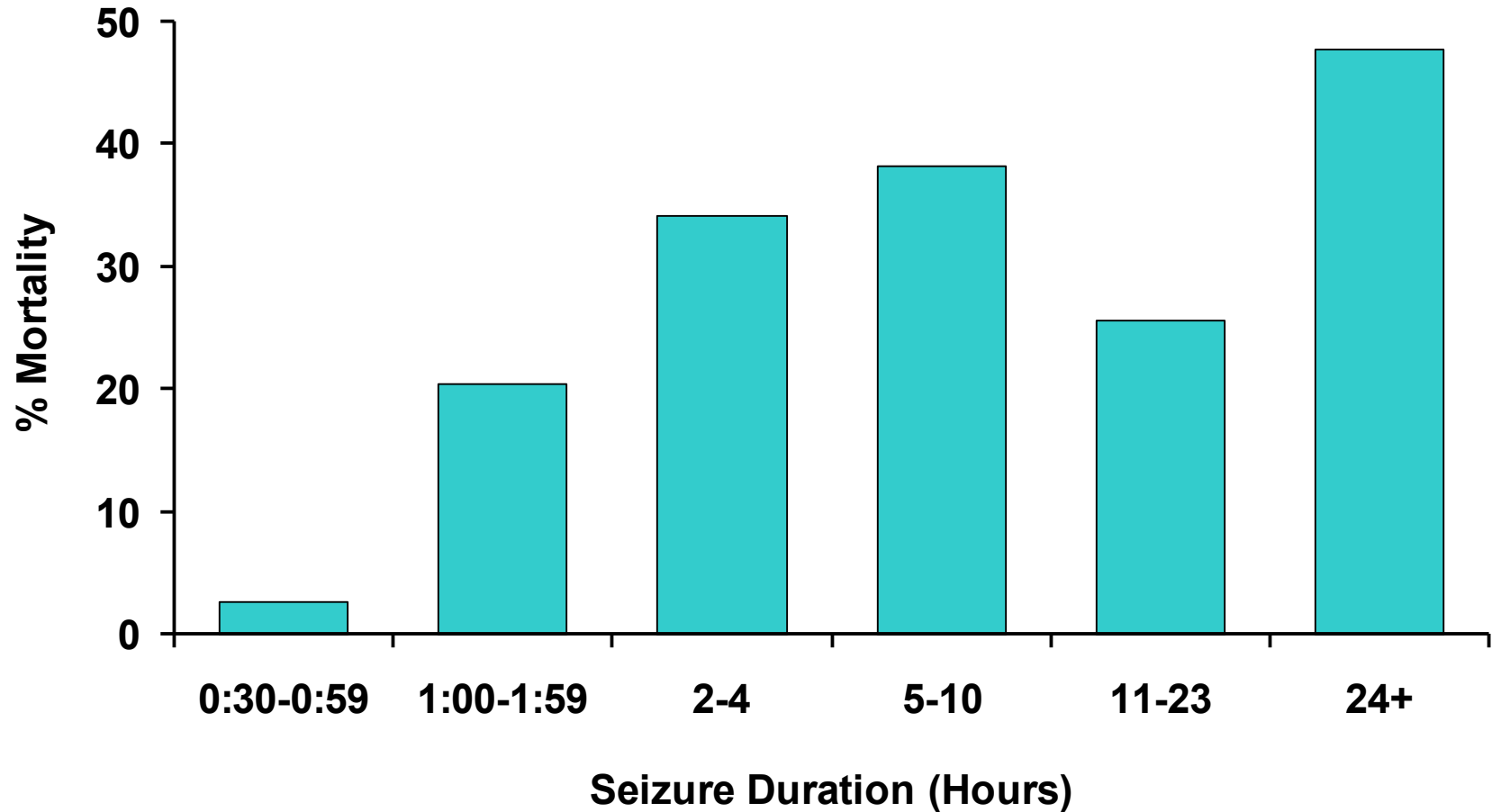
# SE Treatment

- Check emergency ABC's
- Give O2
- Obtain IV access
- Begin EKG monitoring
- Check fingerstick glucose
- Draw blood for KFT, 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.

# SE Treatment Algorithm



# Mortality of SE by duration



# Errors in Management causing poor outcomes

- Inadequate anticonvulsant dosage
- Delay in switching to another drug
- Wrong route of administration (intramuscular phenytoin)
- Delay or failure in initiating maintenance anticonvulsants
- Missing and not treating the precipitating and underlying causes and complications
- Delay in providing cardiorespiratory support such as intubation and vasopressor administration.

# Mimics of focal motor SE

- ▶ Asterixis
- ▶ Chorea
- ▶ Clonus (from spasticity)
- ▶ Dystonia
- ▶ Hemiballismus
- ▶ Myoclonus (brainstem, spinal)
- ▶ Posturing movements (decerebrate and decorticate)  
signs of cerebral herniation
- ▶ Psychogenic non-epileptic seizures
- ▶ Release signs
- ▶ Semi-purposeful activity, for example, picking at objects
- ▶ Spinal reflexes
- ▶ Tremor

## **Box 1: Mimics of generalised convulsive status epilepticus**

- Psychogenic status epilepticus
- Decerebrate spasms
- Tetanus
- Malignant hyperthermia
- Malignant neuroleptic syndrome
- Paroxysmal dyskinesia
- Acute chorea, ballismus, dystonia