SEIZURES, SEIZURE MIMICS, AND EPILEPSY

Sara Molisani, MD
Pediatric Neurology & Epilepsy Attending Physician
Associate Professor
Children's Hospital of Philadelphia
10.16.25

NO DISCLOSURES

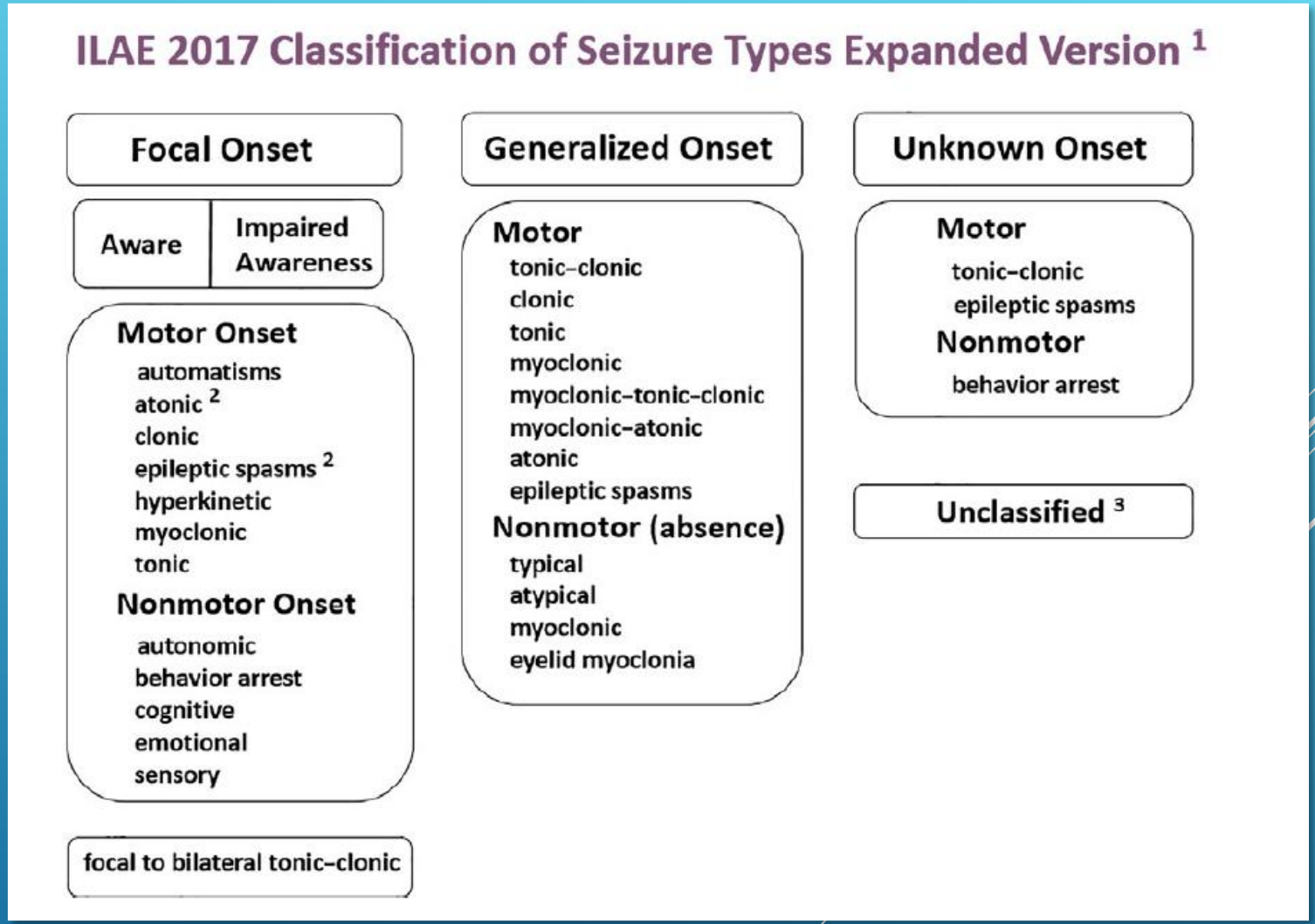
LEARNING OBJECTIVES

1. Learn how to distinguish epileptic seizures from non-epileptic events.
2. Review appropriate diagnostic evaluation of new onset seizure(s).
3. Understand epilepsy diagnostic criteria and classification scheme.

SEIZURES AND SEIZURE MIMICS

SEIZURE

- Transient occurrence of signs / symptoms due to abnormal excessive or synchronous neuronal activity in the brain
- Usually a clinical diagnosis



Fisher RS et al. Epilepsia. 2017.

SEIZURE MIMICS

"Non epileptic events"

"Paroxysmal events"

"Spells"

Not everything that shakes is a seizure!

History is essential. Videos are helpful!

Differential diagnosis varies by age.

Newborns & Infants

- Benign nocturnal myoclonus
- Jitteriness
- Apnea
- Normal movement
- Hyperekplexia
- Movement disorders
- Shuddering spells
- Reflux / Sandifer's syndrome

Toddlers

- Breath holding spells
- Migraine & migraine variants
- Self stimulatory behavior
- Behavioral staring / inattention
- Movement disorders
- Tic disorders
- Stereotypies

Older children

- Syncope
- Behavioral staring / inattention
- Tics / Tourette's
- Stereotypies
- Psychogenic non-epileptic events
- Movement disorders
- Parasomnias
- Narcolepsy with cataplexy

- 14yo F with anxiety and depression presents after an episode of concern.
- Mom heard a thump from the bathroom, where she finds the patient with full body stiffening and shaking, eyes open, unresponsive, and with perioral cyanosis. Duration: ~3-4 min. Afterwards, she is sleepy for a couple hours.

CASE #1

- Seizure
- Convulsive syncope
- Psychogenic non-epileptic event

DIFFERENTIAL DIAGNOSIS

Diagnosis:
Seizure – bilateral tonic clonic seizure

SYNCOPE

- Sudden brief loss of consciousness and postural tone due to transient decrease in cerebral blood flow
- Can be “convulsive” – stiffening +/- shaking of extremities
- Key points to distinguish from seizure:
  - Prodrome of feeling light headed / dizzy – tunnel vision, pallor, hot/cold, clammy, nausea
  - Eyes closed
  - Prompt return to baseline – confusion for no more than seconds/minutes afterwards
  - Precipitating factors

PSYCHOGENIC NON-EPILEPTIC EVENT (PNEE)

- Functional episodes resembling seizures that are non-epileptic
- No ictal correlate if events are captured on EEG.

Clinical feature	Generalized tonic-clonic epileptic seizures	Convulsive functional seizures
Frequency	Variable	Infrequent convulsive functional seizures are unusual
Duration	Usually <2 min excluding postictal phase	Brief convulsive functional seizures are unusual
Eyes	Open/half open	Usually closed
Motor activity	Generalized tonus followed by generalized clonic activity	Alternating movement or tremor, occasionally thrashing, back arching, side-side head movement; tonic features uncommon
Vocalization	Initial, inarticulate, no emotional features	During and after seizure, conveys distress
Autonomic signs	Cyanosis	Signs of arousal and hyperventilation, flushed, pale
Postictal phase	Drowsy, confused, sleeps, severe headache	Often back to alertness quickly; distress
Incontinence of urine	Reported and observed	Commonly reported
Sleep events	Commonly reported/observed, events may occur only during sleep	Commonly reported/observed, but not EEG verified; events reported to occur during sleep only highly unusual
Injury	Commonly reported/observed	Less commonly reported/observed
Burns	Thermal	Friction
Tongue/mouth injury	Bite to lateral tongue or inside of cheek, observed injury	Reported bite to tip of tongue
Stereotypy	Usual	Common

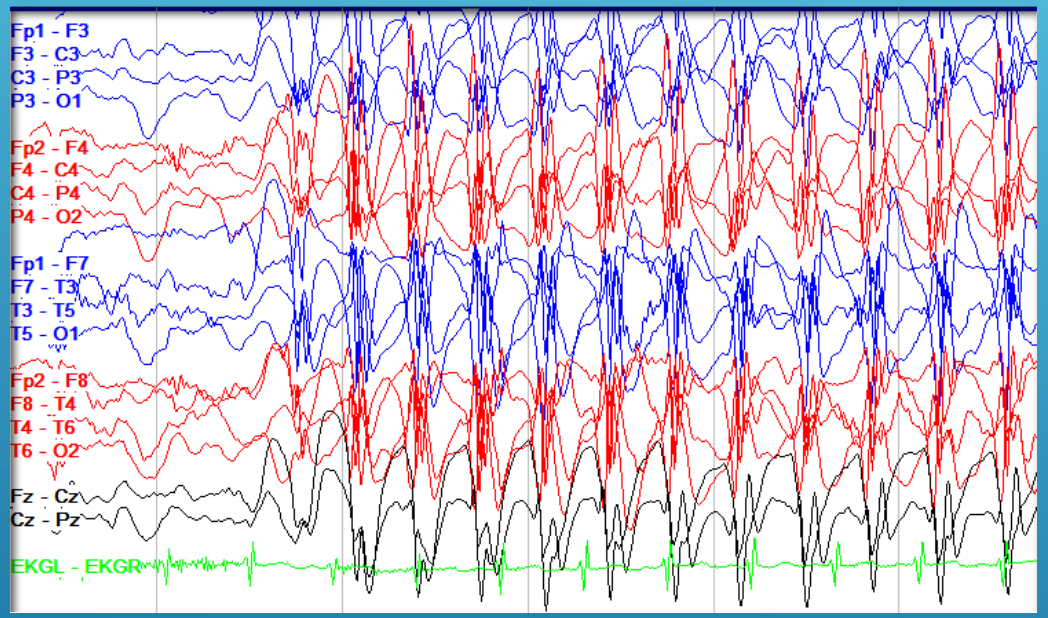
Not all features distinguish between tonic-clonic seizures and the convulsive type of functional seizures; no single feature is sufficiently sensitive or specific to be used alone.

CASE #2

- 6yo healthy M presents for recurrent episodes of staring, repetitive blinking, lip smacking x4-5 seconds, happening multiple times per day.

DIFFERENTIAL DIAGNOSIS

- Behavioral staring
- Tic disorder
- Seizures
  - Absence seizures
  - Focal impaired awareness seizures



DIAGNOSIS: CHILDHOOD ABSENCE EPILEPSY

- Common pediatric epilepsy syndrome
  - 10-17% of all children with epilepsy
- Demographics:
  - Onset: 4-10 years, peak 6-7 years
  - F>M
  - Typically in a normally developing and otherwise healthy child
- Absence seizures:
  - Staring, lack of responsiveness; sometimes with upward eye roll, eye blinking, motor automatisms
  - Duration: seconds
  - Many times per day
  - Provoked by hyperventilation
- GTCs may develop in 40% (may be lower)

FOCAL IMPAIRED AWARENESS SEIZURES

Not all staring seizures are "absence" seizures, a generalized seizure type. Focal seizures can cause staring as well.

Important to distinguish due to implications for diagnosis, testing, treatment options, and prognosis.

	Absence	Focal impaired awareness
Demographics	Tend to occur in school age children (CAE) or adolescents (JAE)	Any age
Semiology	Eye roll, eye flutter, staring	May have aura, may have focal features (asymmetric motor signs)
Frequency	More frequent (numerous/day)	Less frequent
Duration	Tend to be shorter (seconds)	Can be longer (minutes)
EEG	Generalized discharges, 3 Hz spike-wave, often capture absence seizures, particularly during hyperventilation	Focal EEG abnormalities, less likely to capture seizures on routine EEG
Imaging	Not necessarily indicated	Important to assess for seizure focus

BEHAVIORAL STARING

- Can be inattention, such as in setting of ADHD
- Key questions:
  - **Are the episodes consistently interruptible?**
  - **Does the child react to touch during these events?**
- Tends to occur in certain contexts
  - Seizures happen regardless of boredom, specific situations, etc

TIC DISORDER

- Tic: brief, purposeless, stereotyped movement or sound
  - Can be simple or complex
  - Wax/wane in frequency/severity

- Distinguishing from seizures:
  - Premonitory urge
  - Temporarily suppressible
  - No impaired awareness

CASE #3

- 6 month old baby with 2 weeks of episodes of bilateral arm extension lasting a couple of seconds.

DIFFERENTIAL DIAGNOSIS

- Infantile spasms
- Stereotypy
- Shuddering spell
- Reflux / Sandifer's syndrome

Less likely Ddx for this case

Other considerations for baby Ddx:

- *Jitteriness*
- *Sleep myoclonus*

INFANTILE SPASMS

- Sudden bilateral flexion and/or extension, often with forward head nod
- Duration: 1-2 seconds
- Tends to cluster
- Often at times of sleep transition
- Often followed by crying

- Characteristic EEG finding: hypsarrhythmia
- Outcomes:
  - Epilepsy 50-70%
  - Lennox Gastaut Syndrome (LGS) 20-50%
  - Learning difficulties 70-90%
  - Autism 9-35%

Prompt diagnosis and treatment is essential!

STEREOTYPIES

- Repetitive, purposeless movements
- Often start in toddler years
- Can be suppressed
- Can be triggered by excitement, boredom, stress, concentration
- Can occur in children with neurodevelopmental differences or normally developing children
- Examples: shaking, flapping, clenching, stiffening

SHUDDERING SPELLS

- Brief spell of tremoring of the head / upper body
- Shiver type movement
- Duration: few seconds
- More common when excited or upset
- Outgrown with time

JITTERINESS

- Low amplitude, high frequency shaking or tremulousness
- Can be provoked by stimuli (noise, touch)
- Suppressible
- Neonatal phenomenon, can be more common for babies with HIE or NAS
- Improves/resolves with time

SLEEP MYOCLONUS

- Quick jerks of limbs during sleep
- Typically early stages of sleep
- Myoclonic jerks do not consistently occur in same extremity
- Can occur at any age
  - In babies: Benign infantile sleep myoclonus

REFLUX / SANDIFER SYNDROME

- Episodes of stiffening and/or posturing due to reflux
- Spells tend to occur shortly after feeding

EVALUATION OF NEW ONSET SEIZURE(S)

WORK UP OF FIRST UNPROVOKED SEIZURE

- History
- Exam
- EEG
- +/- Imaging
- +/- Other: labs, genetics

HISTORY: DETAILED EVENT DESCRIPTION IS KEY

Suppressible?

Interruptible?

Eyes open or closed?

Post ictal state?

Stereotyped?

Typical for a seizure semiology?

Any provoking factors?

Hypoglycemia, toxic ingestion, CNS infection, trauma

Illness, fever, certain medications, sleep deprivation

Videos are extremely helpful!

HISTORY

- Birth history
  - Any perinatal insult?
- Developmental history
  - Normal or abnormal development?
  - Any regression?
- Family history
  - Seizures/epilepsy?

EXAMINATION

- Mental status (acute setting)
- General: Dysmorphic features
- Skin: Stigmata of neurocutaneous syndromes
- Head circumference
- Fundoscopic examination: Papilledema
- Neurologic examination: Focal neurologic deficits, Muscle tone

14yo F with anxiety and depression presenting after first time event of full body stiffening, shaking, unresponsiveness x3-4 minutes followed by sleepiness for a couple hours.

- Additional history:
  - No other similar prior events
  - No provoking factors.
  - Returned completely to baseline after ~2 hours following event.

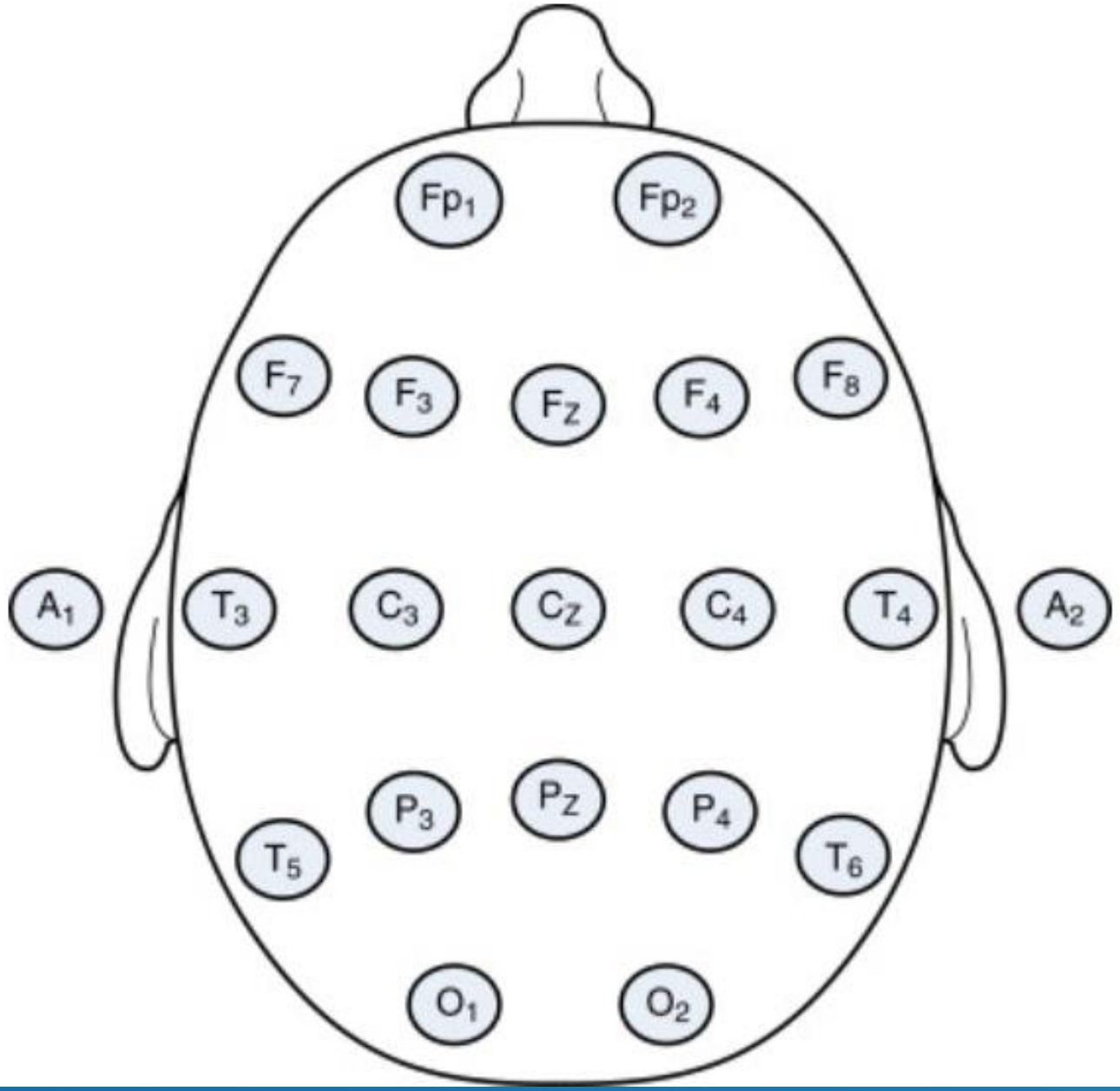
- Birth history: FT, healthy pregnancy & delivery
- Developmental history: Normal
- Family history: No relevant FHx
- Examination: Normal

CASE #1, CONTINUED

Diagnosis: First unprovoked seizure
Any testing needed?

EEG

- Records electrical activity from the cortex via scalp electrodes
- 10-20 International System of Electrode Placement



Libenson M. Practical Approach to Electroencephalography. 2010.

EEG

- Recommended for all children after a first unprovoked seizure.

- Helpful for:
  - Confirmatory evidence in support of a diagnosis of epilepsy
  - Considering recurrence risk after a first seizure
  - Determining epilepsy / seizure type
  - Determining epilepsy syndrome (if applicable)

- Informs:
  - Need for imaging studies
  - Choice of med (if applicable)

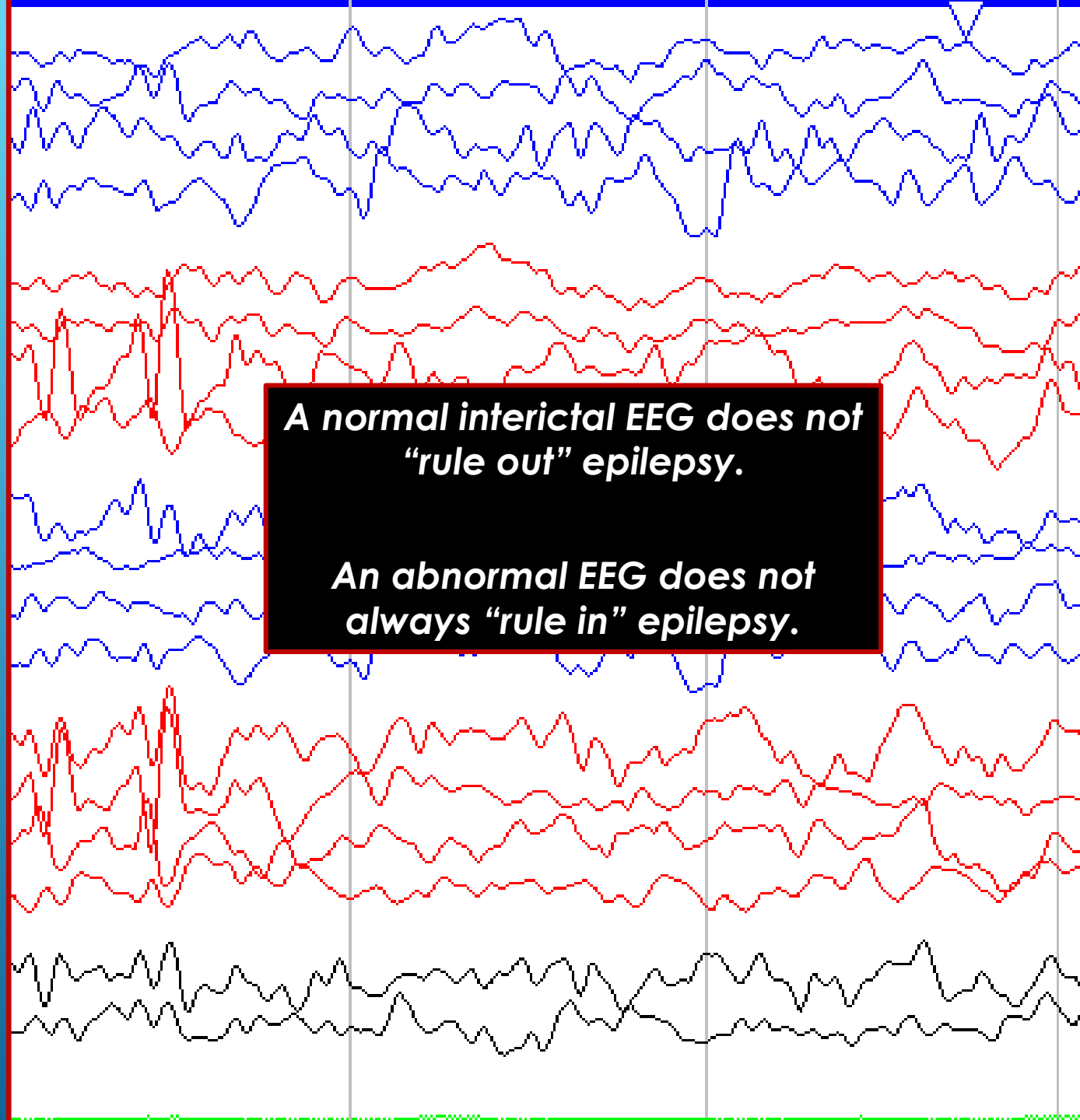
EEG CONSIDERATIONS

Timing:

- Within 1-2 days of seizure:
  - More likely to see an abnormality
  - Also more likely to see post-ictal slowing
  - Interpret with caution!
- Ideal timing is not known
- Likely okay to get on an outpatient basis

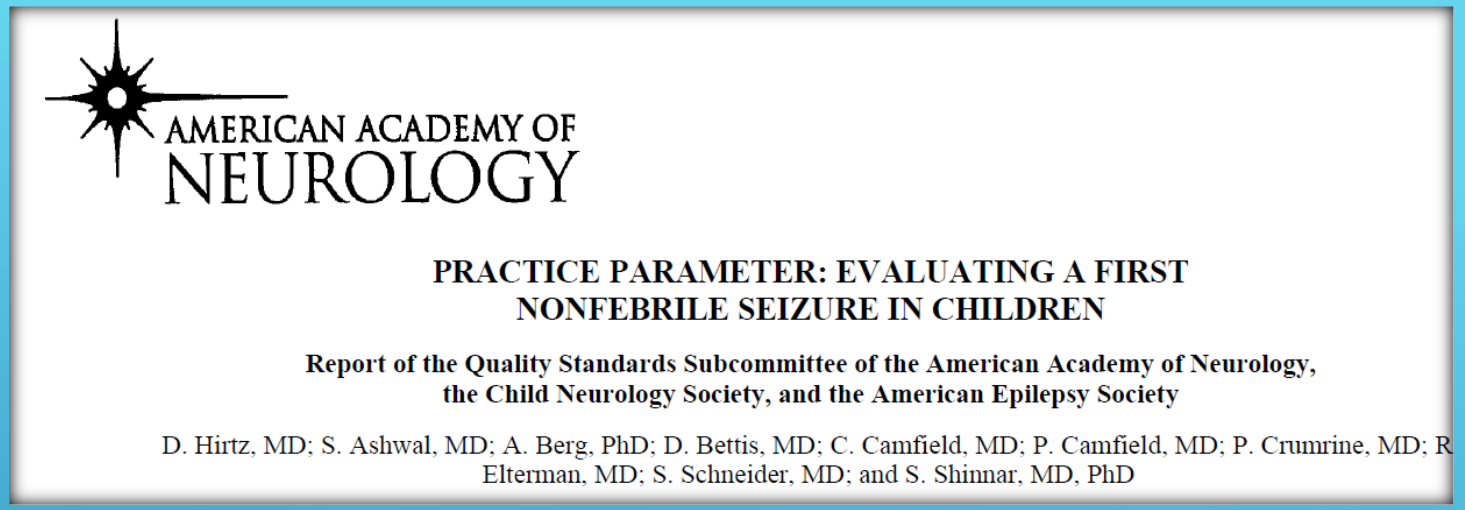
EEG abnormalities:

- 3-5% of children without epilepsy can have epileptiform abnormalities on EEG
- 40% of children with chronic epilepsy do not have abnormalities on EEG



IMAGING

- Emergent neuroimaging if:
  - Focal deficit on neurologic examination
  - Signs of increased intracranial pressure
  - Not returning to baseline following seizure
- Head CT useful in emergency setting to evaluate for bleed, skull fracture, large tumor
- MRI preferred modality in general for nonurgent imaging
  - Usually indicated unless patient has a benign focal epilepsy syndrome of childhood or a primary generalized epilepsy type

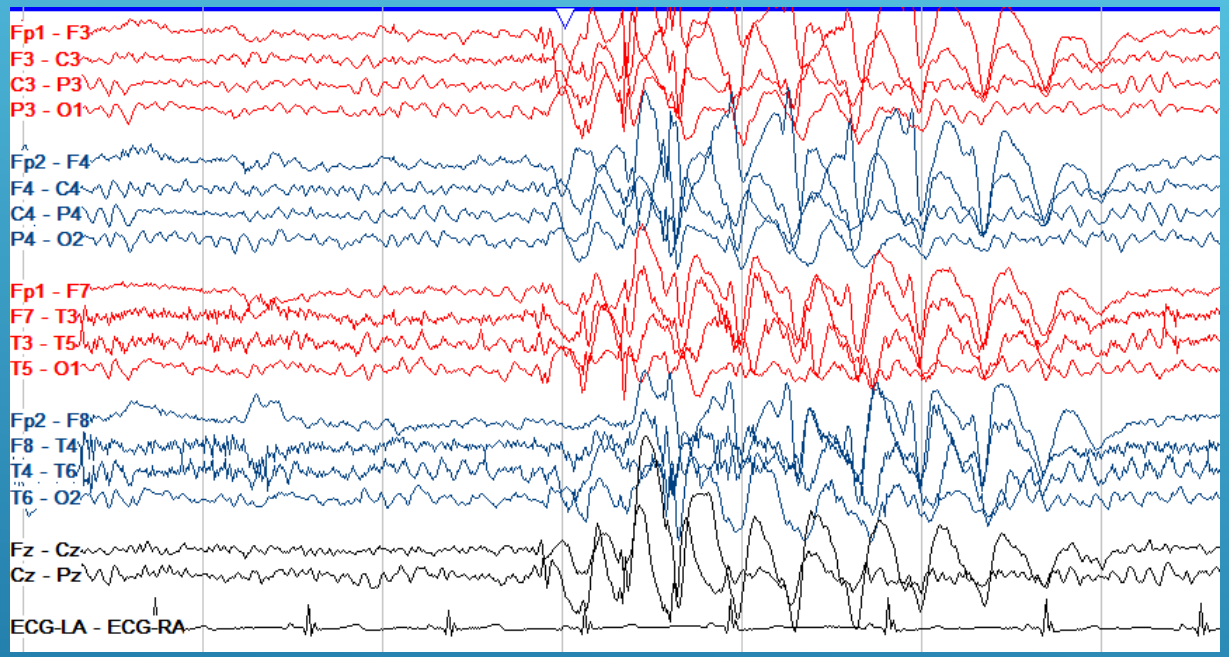


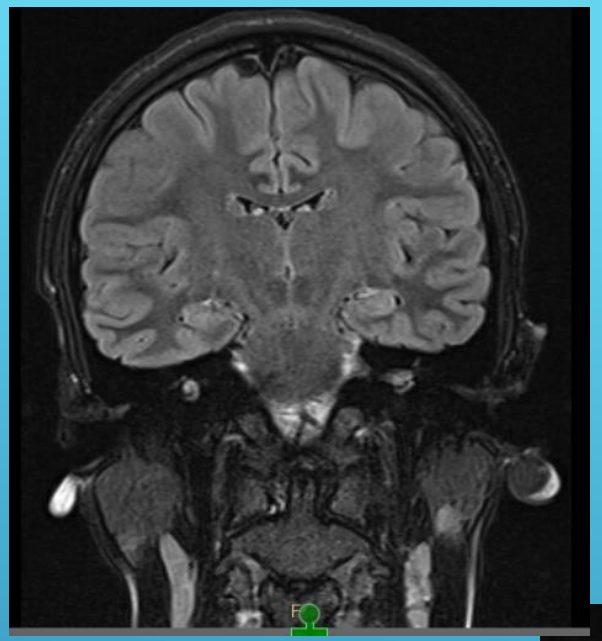
- If guided by clinical picture:
  - Labs: CBC, serum electrolytes, glucose
  - Toxicology screen
  - Lumbar puncture

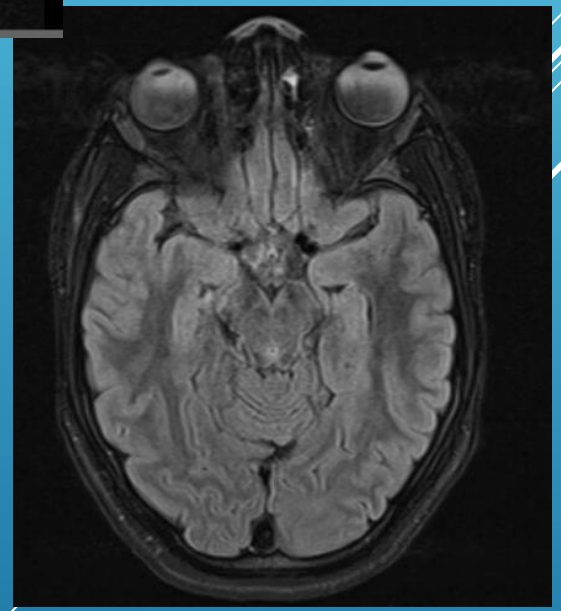
- For most children with a first unprovoked seizure who have returned to baseline, these tests are of limited value.

OTHER TESTING

EPILEPSY







CASE #1, CONTINUED

EEG:

Epileptiform discharges, generalized

Brain MRI:
normal

FIRST UNPROVOKED SEIZURE VS EPILEPSY

1st unprovoked seizure

- 50% chance of future unprovoked seizures

2nd unprovoked seizure

- 70-80% chance of future unprovoked seizures

Epilepsy:

An enduring predisposition to have epileptic seizures

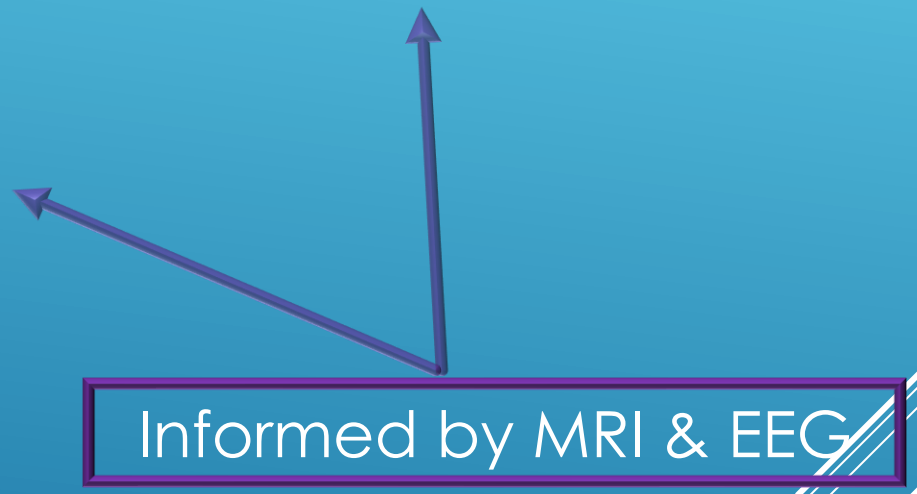
EPILEPSY: ILAE DEFINITION (2014)

At least one of the following:

≥2 unprovoked (or reflex) seizures occurring >24 hours apart

1 unprovoked (or reflex) seizure and a probability of further seizures > 60%

Diagnosis of an epilepsy syndrome



EPILEPSY CONSIDERATIONS

Type

- Focal
- Generalized
- Combined
- Undetermined

Etiology

- Structural
- Genetic
- Idiopathic
- Metabolic
- Immune/inflammatory
- Infectious

Control

- Well controlled
- Drug resistant

CASE #1, CONTINUED

- Second unprovoked seizure occurred 6 weeks later with same presentation.
- Epilepsy diagnosed.
  - Epilepsy type: Generalized
  - Seizure type: Generalized tonic-clonic
  - Etiology: Suspected genetic
- Treatment:
  - Daily anti-seizure medication: levetiracetam
  - Seizure rescue medication: intranasal midazolam PRN seizure > 5 minutes

TREATMENT OF SEIZURES & EPILEPSY

SEIZURE SAFETY

- Water safety
  - No unsupervised swimming or bathing
- Heights
  - Avoid extreme heights
- Sports / activities
  - Use applicable protective gear (helmet for bike riding, etc)
- Driving laws
- General mindfulness about other safety considerations (ex: fire safety)

SEIZURE FIRST AID

Epilepsy.com

HOW DO WE TREAT?

- Recommend starting daily anti-seizure medication ***once epilepsy is diagnosed***
- Ideal goal:
  - No seizures
  - No side effects
- How we choose meds:
  - Focal vs generalized epilepsy
  - Seizure type
  - Side effect profile
  - Monitoring considerations
  - Formulation
  - Interactions

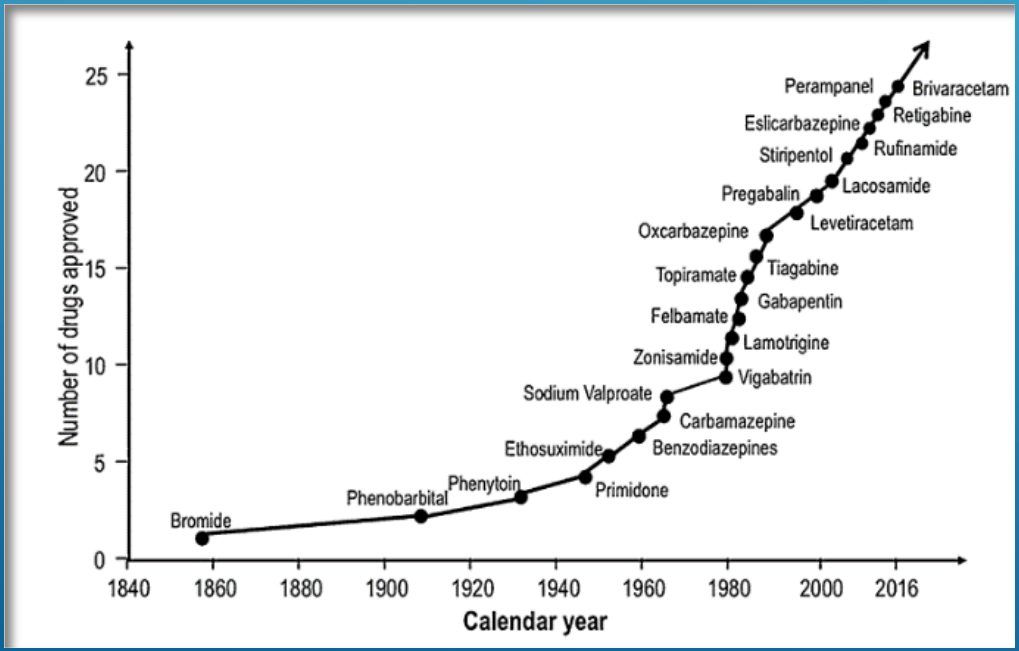
EPILEPSY TREATMENT OPTIONS

Anti seizure medications

Dietary Therapy

Epilepsy surgery

Consider if drug resistant



Golyala A, Kwan P, 2016.

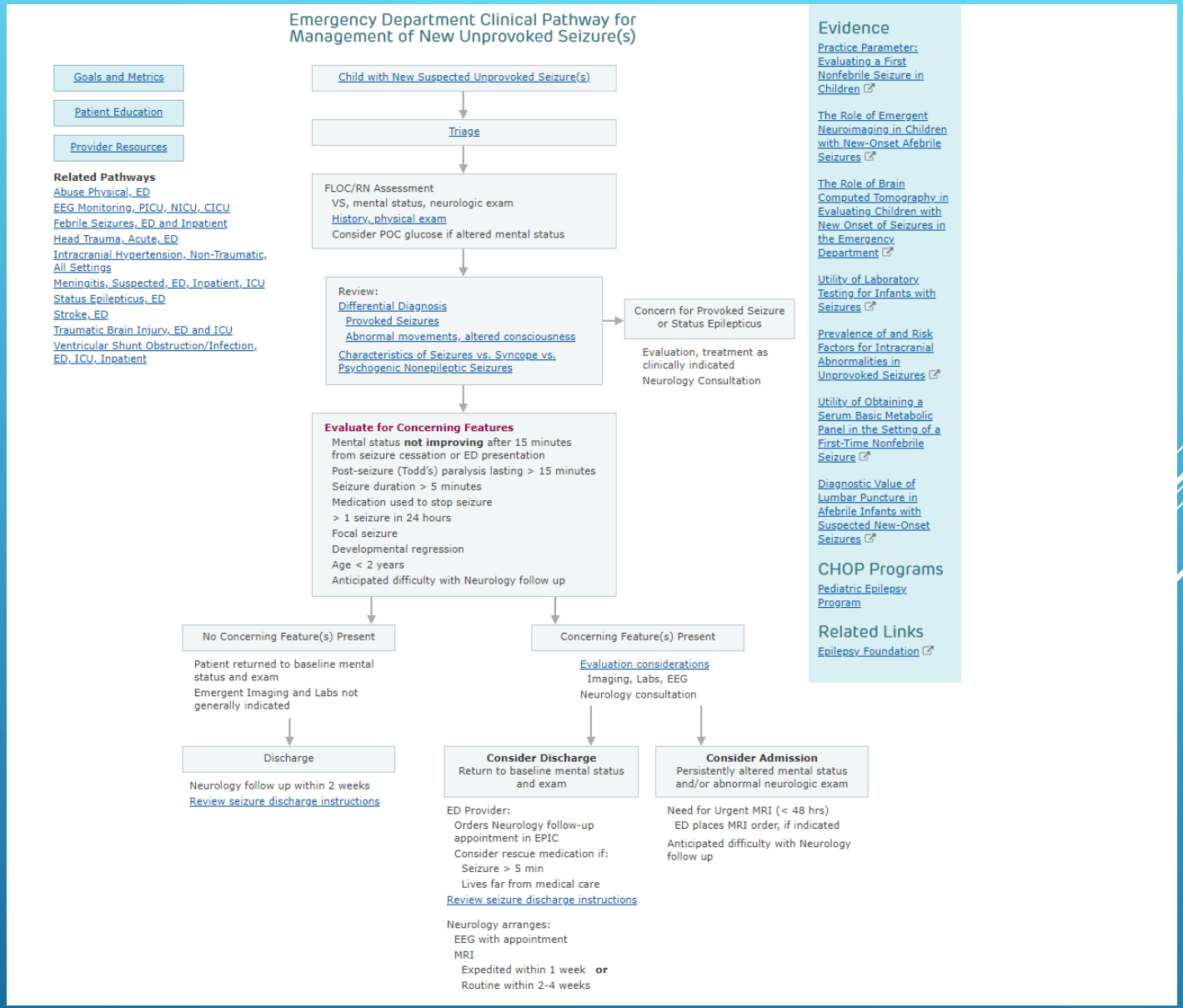
HOME SEIZURE RESCUE MEDICATION

Consider for any child who has had a seizure, particularly if convulsive or prolonged.

Options:			
Rectal diazepam	Intranasal diazepam	Intranasal midazolam	ODT clonazepam

CHOP CLINICAL PATHWAY

Unprovoked Seizure Clinical Pathway — Emergency Department | Children's Hospital of Philadelphia (chop.edu)



TAKE HOME POINTS

- The differential diagnosis for seizures is broad and varies by age group. A good history is essential in narrowing the differential diagnosis.
- Epilepsy can be diagnosed if a patient has had 2 or more unprovoked seizures >24 hours apart, 1 unprovoked seizure and a probability of further seizures > 60%, or a diagnosis of an epilepsy syndrome.
- EEG is often helpful in evaluating possible seizures and/or epilepsy. Neuroimaging (usually brain MRI) is often indicated in the work up as well.

REFERENCES

- Appleton RE. West syndrome: long-term prognosis and social aspects. Brain Dev. 2001; 23(7):688-691.
- Duncan R. Functional seizures: Etiology, clinical features, and diagnosis. UpToDate. Last updated 2025.
- Fisher RS. A practical clinical definition of epilepsy. Epilepsia. 2014; 55(4): 475-482.
- Fisher RS, Cross JH, D'Souza C, French JA, Haut SR, et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia. 2017; 58(4):531-542.
- Gogou M and Cross JH. Seizures and epilepsy in childhood. Continuum. 2022; 28 (2): 428-456.
- Hirtz D, Ashwal S, Berg A, Bettis D, Camfield C, et al. Practice Parameter: Evaluating a First Nonfebrile Seizure in Children. Report of the Quality Standards Subcommittee of the American Academy of Neurology, the Child Neurology Society, and the American Epilepsy Society. Neurology. 2000; 55: 616-623.
- James, Kaitlin C. *Fenichel's Clinical Pediatric Neurology : A Signs and Symptoms Approach /*. Philadelphia, PA : Elsevier, Inc., 2024. Print.
- Libenson M. Practical Approach to Electroencephalography. 2010.