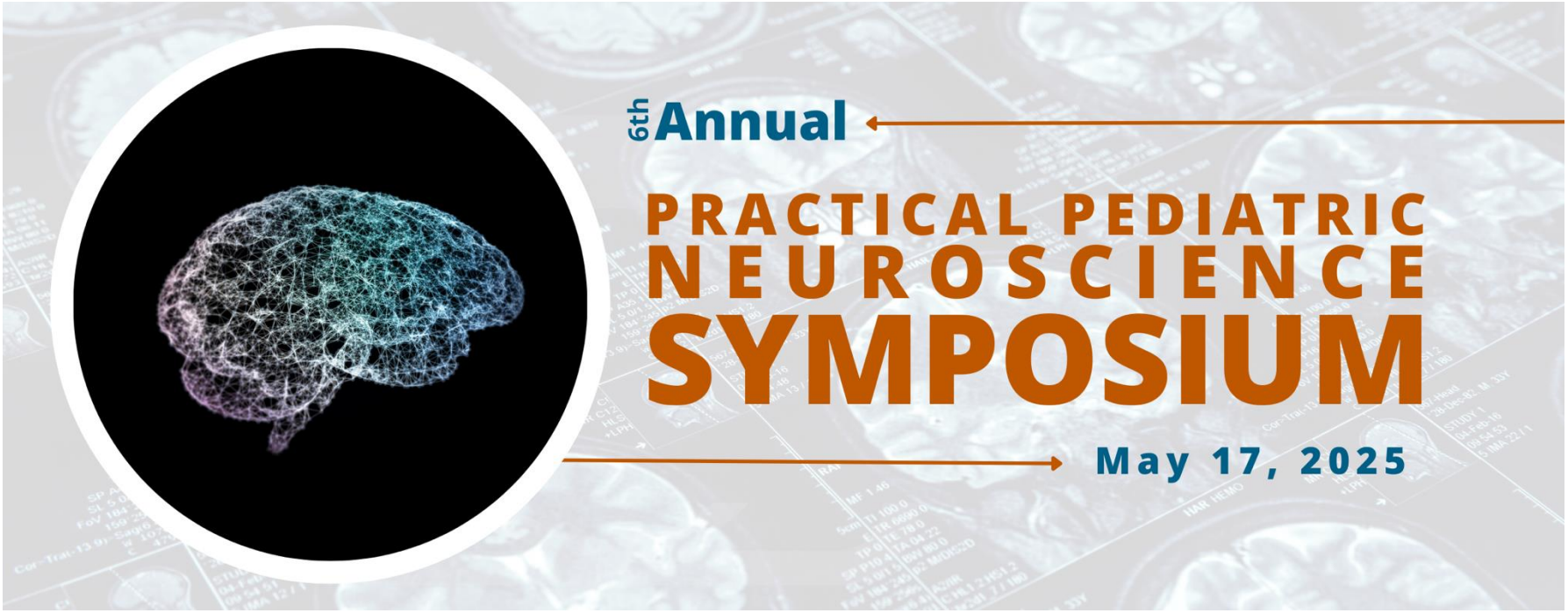

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New-Onset Seizure: From the Teeny-Tiny to the Teen

6th Annual Practical Pediatric Neuroscience Symposium

Clifford Soren Calley, MD
Assistant Professor of Neurology, Neurosurgery, and Pediatrics
Medical Director of The Magnetoencephalography Lab (MEG)
Medical Director of The Transcranial Magnetic Stimulation Lab (TMS)
Dell Medical School | The University of Texas at Austin
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The video of the following presentation has been made available for free by UT Health Austin Pediatric Neurosciences at Dell Children's at:

https://youtu.be/FYI9NIKZ4e0?feature=shared

To see all event presentations, please use this link for the 6th Annual Practical Pediatric Neuroscience Symposium presentation playlist:

https://youtube.com/playlist?list=PLPPnZ7QxWdeR-cpRyBnU2C2eEVh1bW1YR&feature=shared

Interprofessional Continuing Education

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Clifford Calley, MD

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2. I will not discuss off label use and/or investigational use in my presentation.
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INTERPROFESSIONAL CONTINUING EDUCATION

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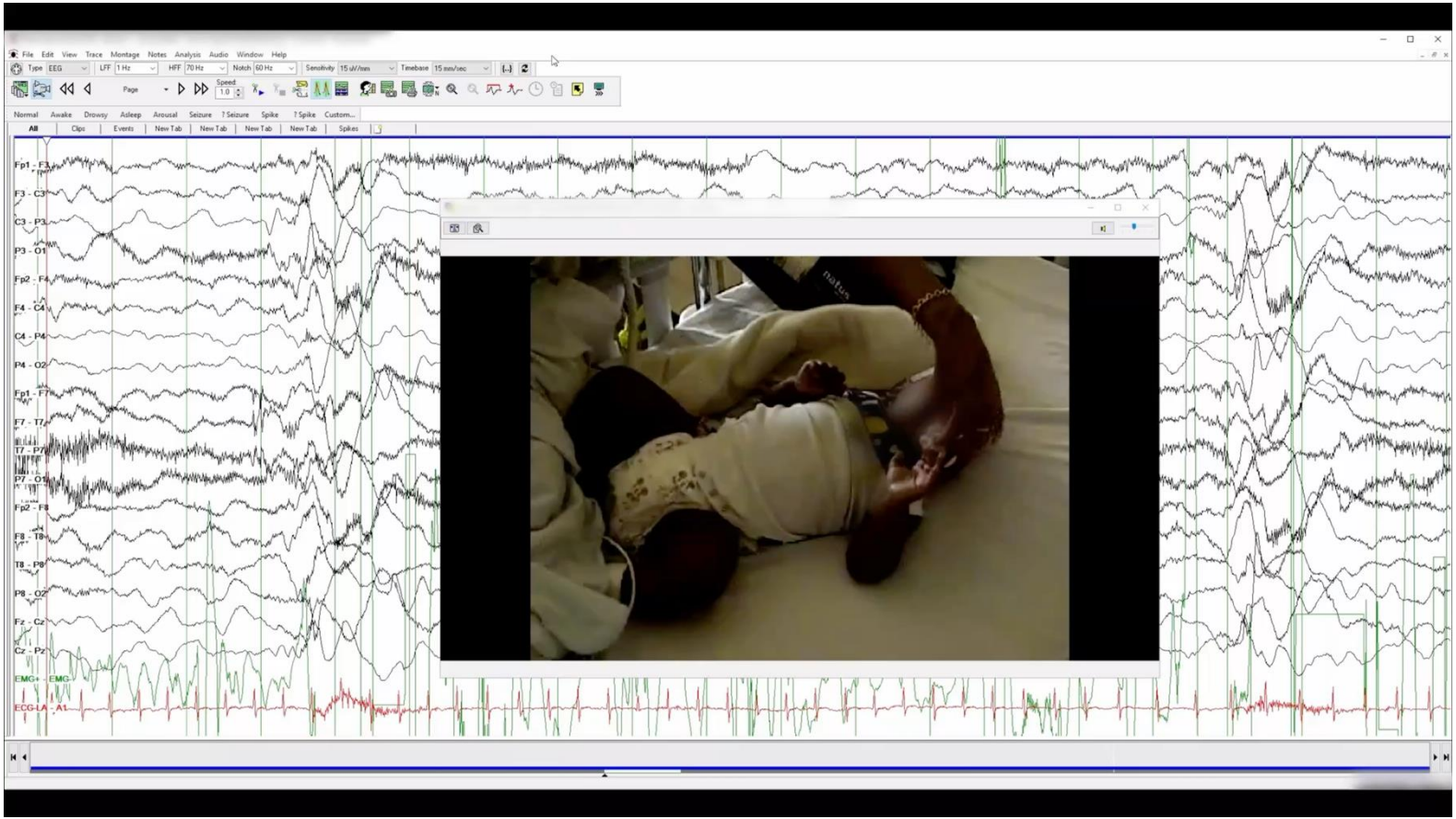
A commercial interest is any entity producing marketing, re-selling, or distributed health care good and services consumed by, or used on, patients.

Case #1

- 5-month-old boy
- Presents to your office with mother for cough, congestion, and several “startle-like” movements that started a few days ago.
- Mother, “Both arms go up, bent at the elbow, and both legs stiffen. His eyes roll back, his head goes back, and his face would ‘squint’ followed by a cry.”
- They happen about 3-5 times over the course of 1-2 minutes.

Case #1

- Born at 36 weeks via emergency c-section due to failure to progress.
- Needed 20 days in NICU for feeding difficulties.
- Not rolling over or able to maintain a sitting position.
- Mom thinks maybe his right arm and leg are stiffer than the left.



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Case #1

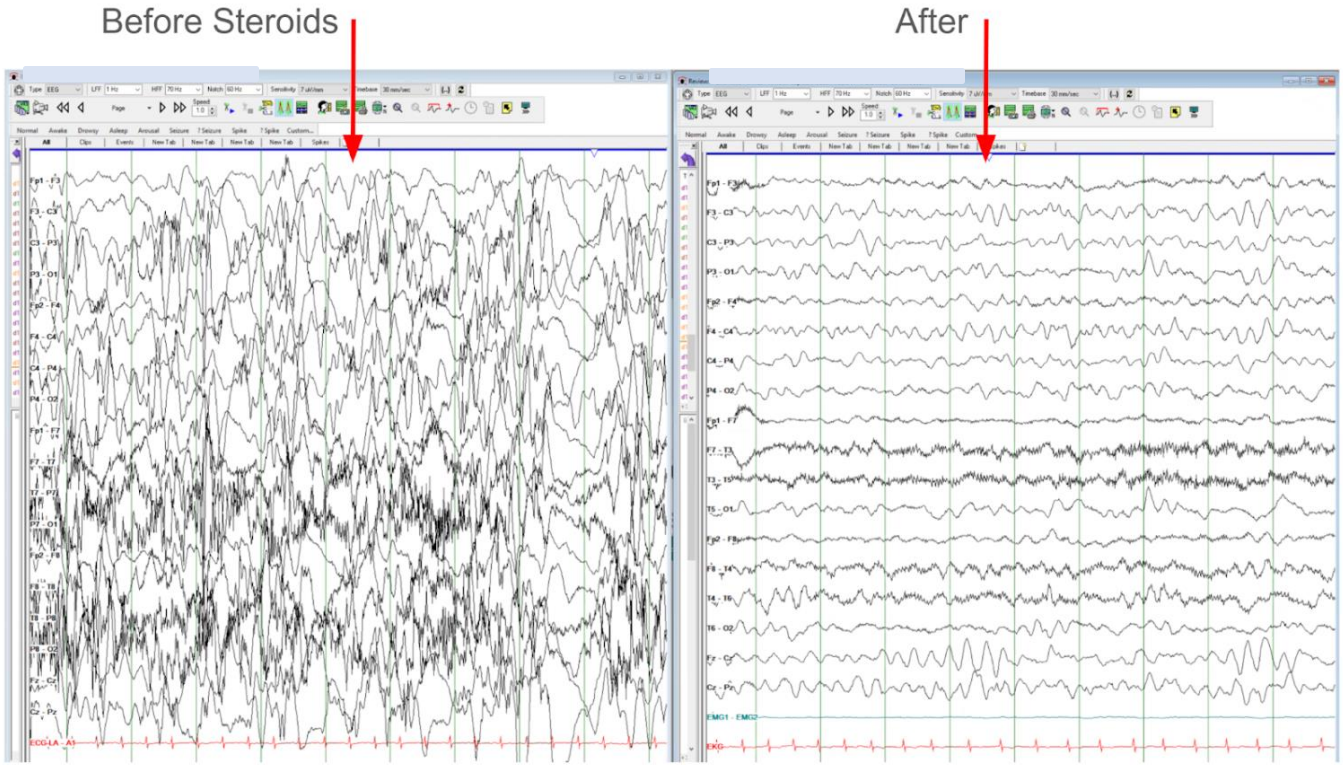
Next steps?

- Manage cough/congestion, follow up next week on startle movements?
- Place referral to your friendly neighborhood neurologist and advocate for earliest possible appointment?
- Make immediate arrangements for evaluation at a children's hospital with EEG capabilities?

Infantile Spasms

- **<u>Early diagnosis and appropriate treatment is critical!</u>**
- 15-20% will progress to Lennox-Gastaut syndrome.
- Age onset: about 4mo - 18mo.
- 1200 new cases in US per year.
- Cause can be found in ~70% of cases:
  - TSC, T21, Aicardi, cortical malformation, infection
- Standard antiseizure medications (ASMs) are not effective
  - Need 1 or more: high-dose steroids, vigabatrin, ACTH

Infantile Spasms



Infantile Spasms: Medication Pearls

High-dose steroids

- Prednisolone 8mg/kg/day (max 60mg)
- Immunocompromised state
- Follow up with PCP after 1st week to check BP
- Placed on GI prophylaxis

Vigabatrin

- Gaba-transaminase irreversible inhibitor
- Permanent concentric visual field constriction; reversible MRI hyperintensity in thalamus, basal ganglia
- Risk evaluation and mitigation (REMS) program required for prescribers, patients, and pharmacies

ACTH

- 97,000% price hike; typical single course median cost $96,406
- Prednisolone is just as effective

Case #2

- 2yo term girl presents to your office with her parents.

- Mother says, “My baby is having seizures and Google tells me they are something called infantile spasms. I’ve now gone down the Google rabbit hole and am incredibly worried. Is my baby going to die?”

- Mother has videos of the events!

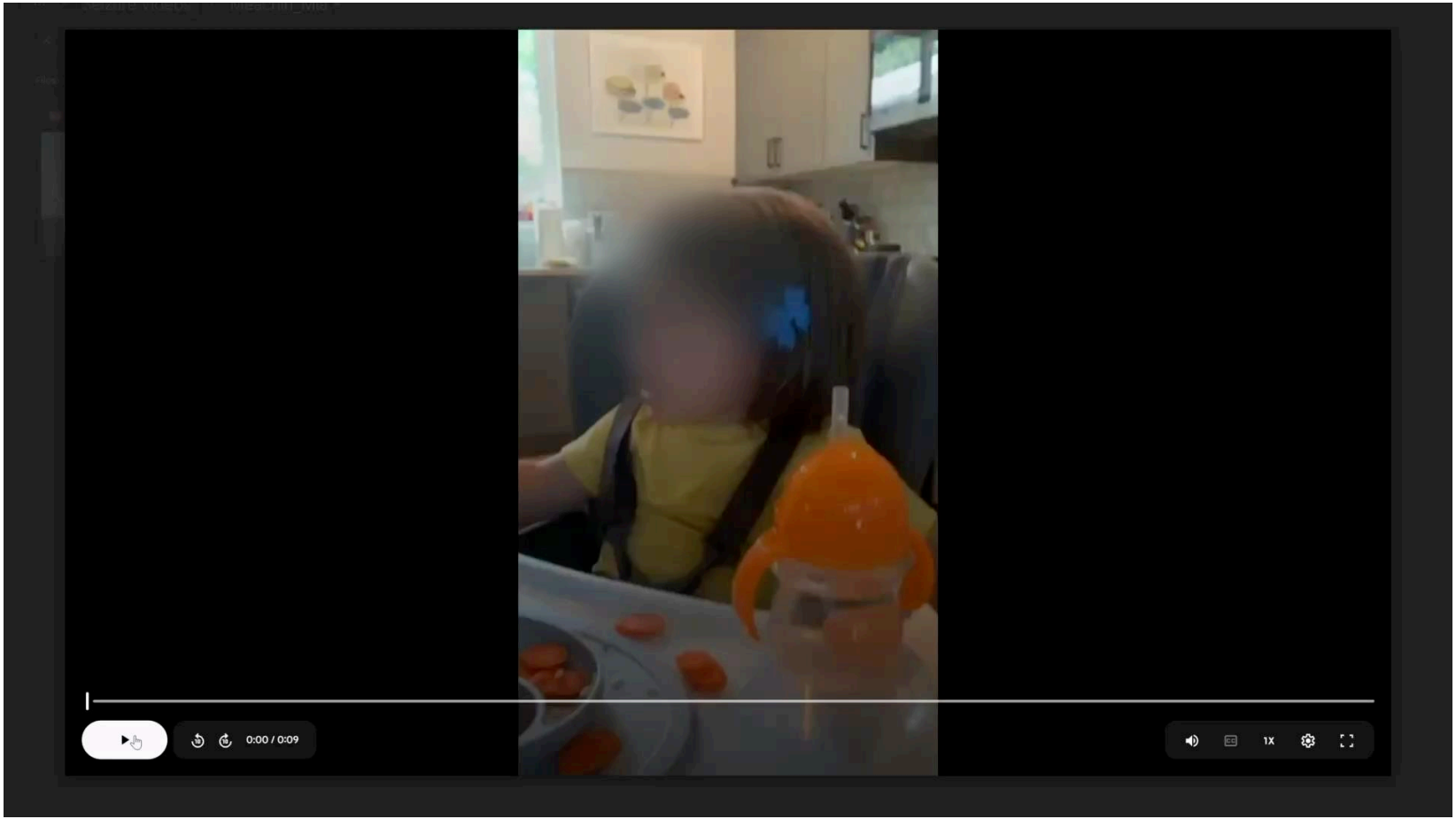
Case #2

Events:

- Clusters of brief head and shoulder twitching with facial grimacing.
- Her face becomes red but events do not seem to bother her.
- Only occur when she is unengaged in activities.
- Events are interruptible.

Case #2

- Born at term, spontaneous vaginal delivery, no complications.
- No concern for developmental delay currently.
- No family history.
- Patient is an only child.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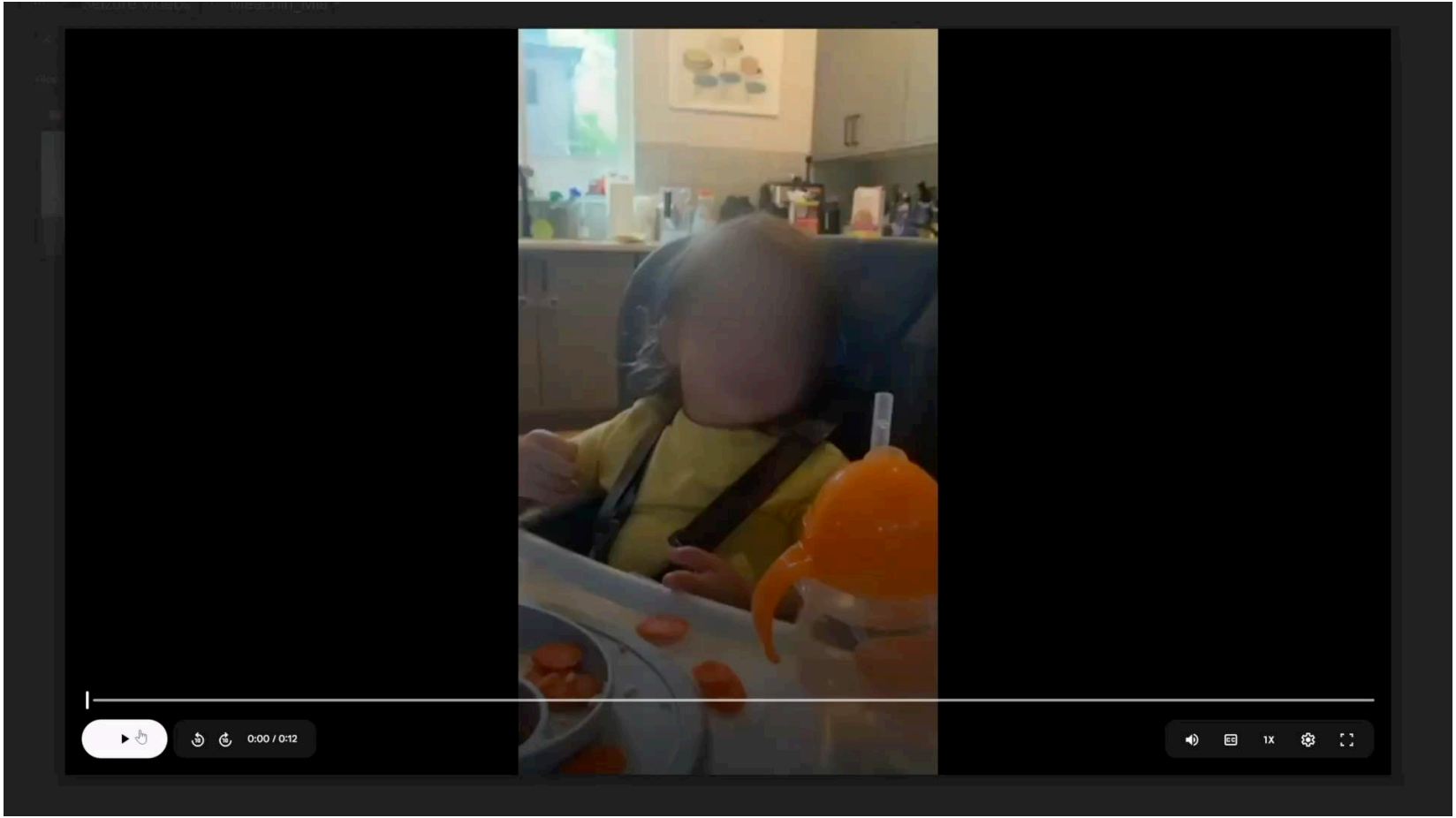
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Case #2

Next steps?

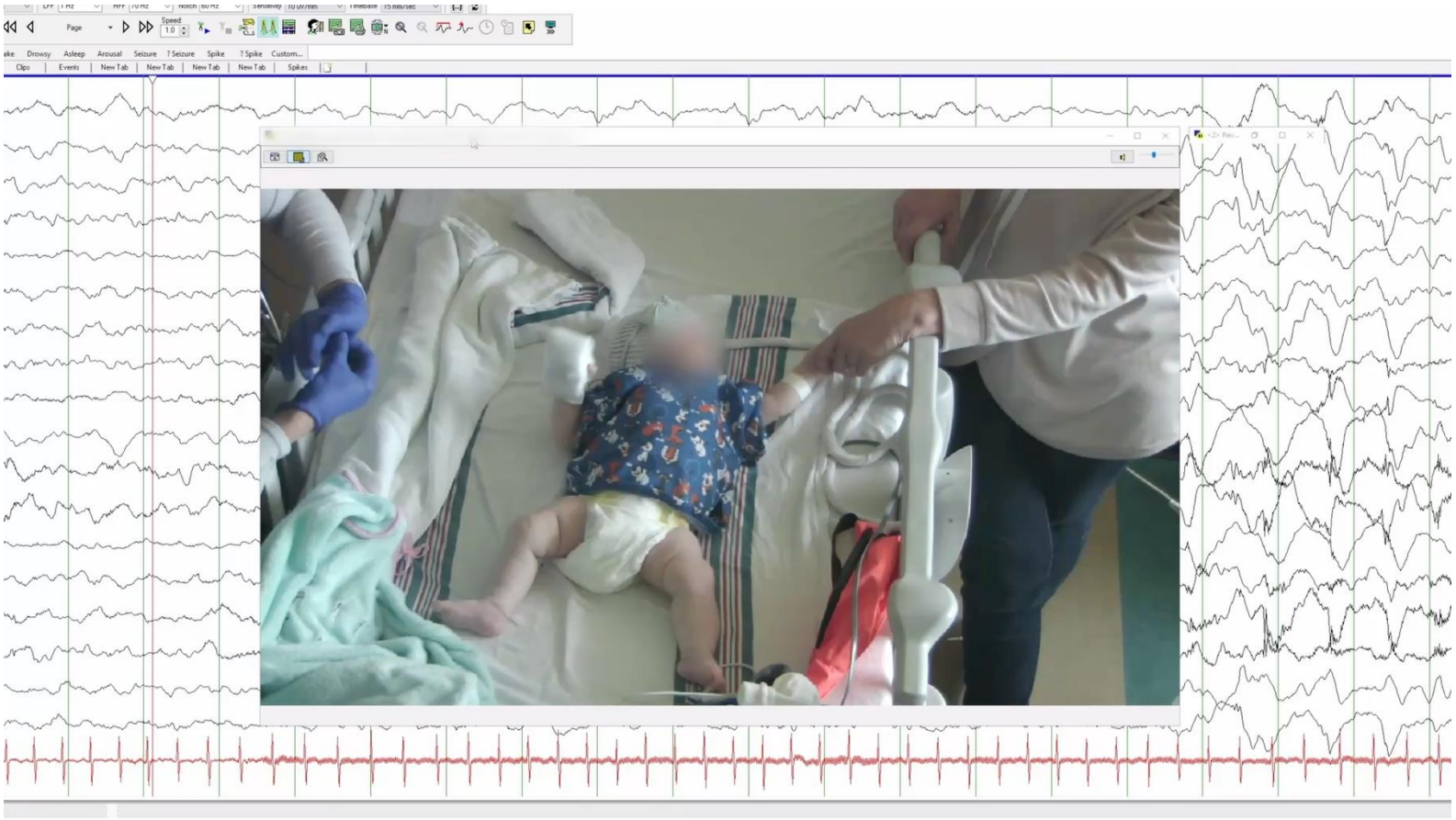
- Provide reassurance and plan for follow-up in 12 weeks?
- Place referral to your friendly neighborhood neurologist?
- Make immediate arrangements for evaluation at a children's hospital with EEG capabilities?

Reassurance

- Video is consistent with a benign paroxysmal spell likely induced by overstimulation.
- This is normal behavior that, with redirection, can be extinguished over time.
- Events did not upset patient, were too sustained for spasms, were interruptible, and only occurred in specific settings.
- Referral to neurology for further reassurance/confirmation is not a wrong answer.

Case #3

- 1mo term baby, no significant birth history, doing well until a few days ago.
- Presents to your office with mother and father for concerning movements.
- Parents report events of rhythmic twitching of whole body, maybe worse on right side, during which baby is not responsive.
- Parents have a video of the events!



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Focal motor seizures with impaired consciousness

- This infant was later diagnosed with focal cortical dysplasia type 1 located in the frontal and temporal lobes of the left hemisphere.
- Note the rhythmic ~1Hz jerking of the head and extremities (right > left).
- Multiple seizures per day, and episodes of super refractory status epilepticus were seen.
- Now seizure-free x5 months after surgical intervention.

ILAE 2023: Treatment of Seizures in the Neonate: Guidelines and Consensus-Based Recommendations

Recommendations 1: First-line Antiseizure Medication

Evidence-based recommendation:

In neonates with seizures requiring antiseizure medication (ASM), phenobarbital should be the first-line ASM

Strength of Recommendation: **Moderate**

Consensus-based recommendations:

Phenobarbital should be the first-line ASM regardless of etiology (including hypoxic-ischemic encephalopathy, stroke, and hemorrhage).

Level of Agreement: **High**

If channelopathy is likely the cause for seizures due to family history then a sodium channel blocker should be the first-line ASM.

Level of agreement: **High**

Recommendations 2: Second-line Antiseizure Medication

Consensus-based recommendations:

In neonates with seizures not responding to first-line antiseizure medication (ASM), phenytoin, levetiracetam, midazolam, or lidocaine may be used as a second-line ASM for most etiologies (hypoxic-ischemic encephalopathy, stroke, or hemorrhage).

Level of agreement: **Moderate**

If channelopathy as an etiology for the seizures is suspected because of clinical or EEG features, then a sodium channel blocker should be used as a second-line ASM. This should be phenytoin or carbamazepine depending on the clinical state of the neonate (critically ill or otherwise well baby) and the regional availability of ASM and monitoring of drug levels.

Level of agreement: **High**

In a neonate with cardiac disorder(s), levetiracetam may be preferred as a second-line ASM.

Level of agreement: **Moderate**

ILAE 2023: Treatment of Seizures in the Neonate: Guidelines and Consensus-Based Recommendations

Recommendation 3: Duration of ASM treatment

Consensus-based recommendations:

Following cessation of acute symptomatic seizures (electroclinical or electrographic) without evidence for neonatal onset epilepsy, antiseizure medications should be discontinued before discharge home, regardless of MRI or EEG findings.

Level of agreement: **High**

Neonate: Medication Pearls

Phenobarbital

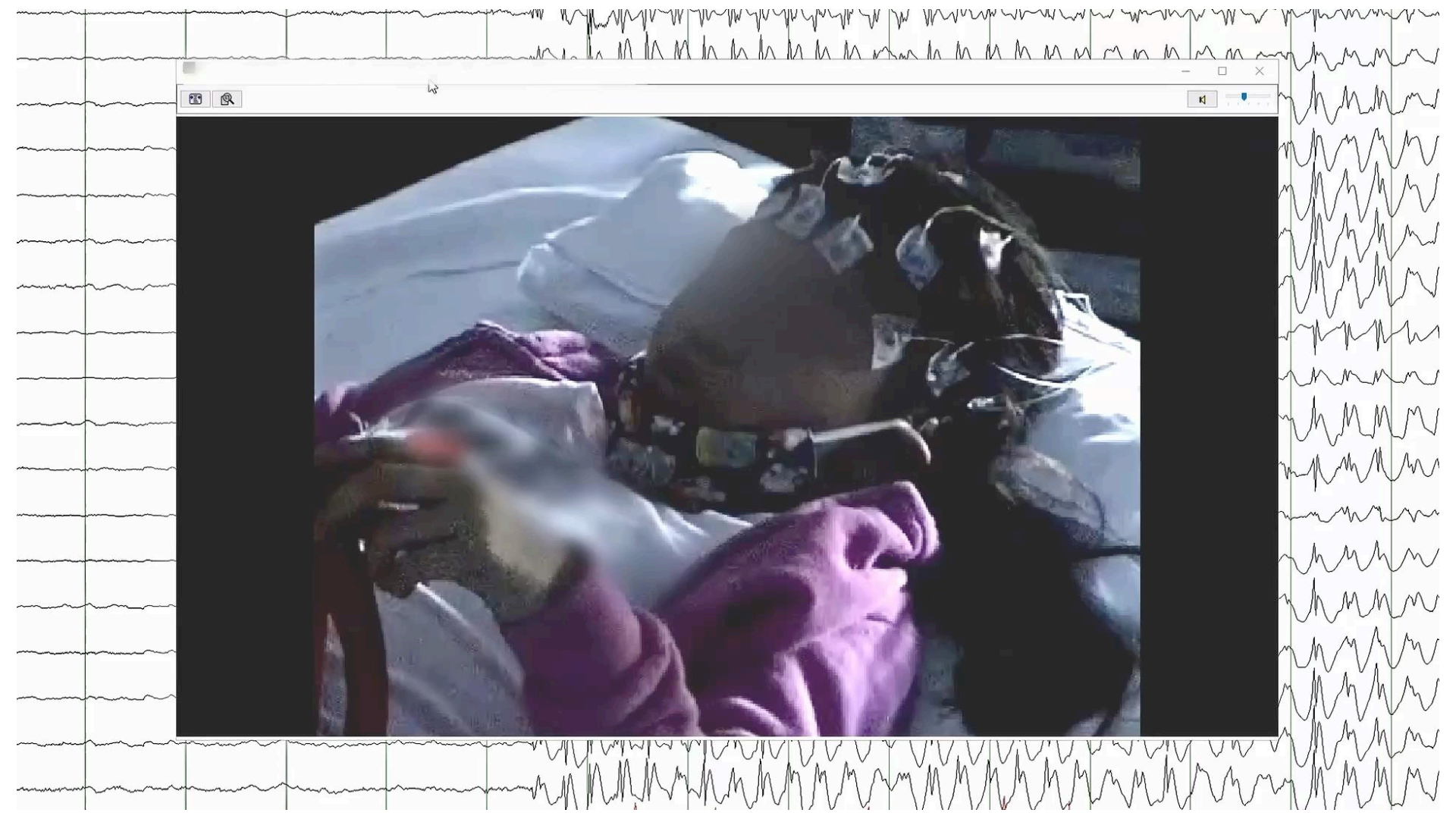
- Neurotoxic with prolonged use.
- Very long half-life.
- Hypotension, bradycardia, respiratory depression.
- CYP450 inducer.

Levetiracetam (Keppra)

- Excellent safety profile even at high doses.
- Irritability (sometimes severe); can mitigate with vitamin B6.
    - In older patients with irritability, can try brivaracetam.

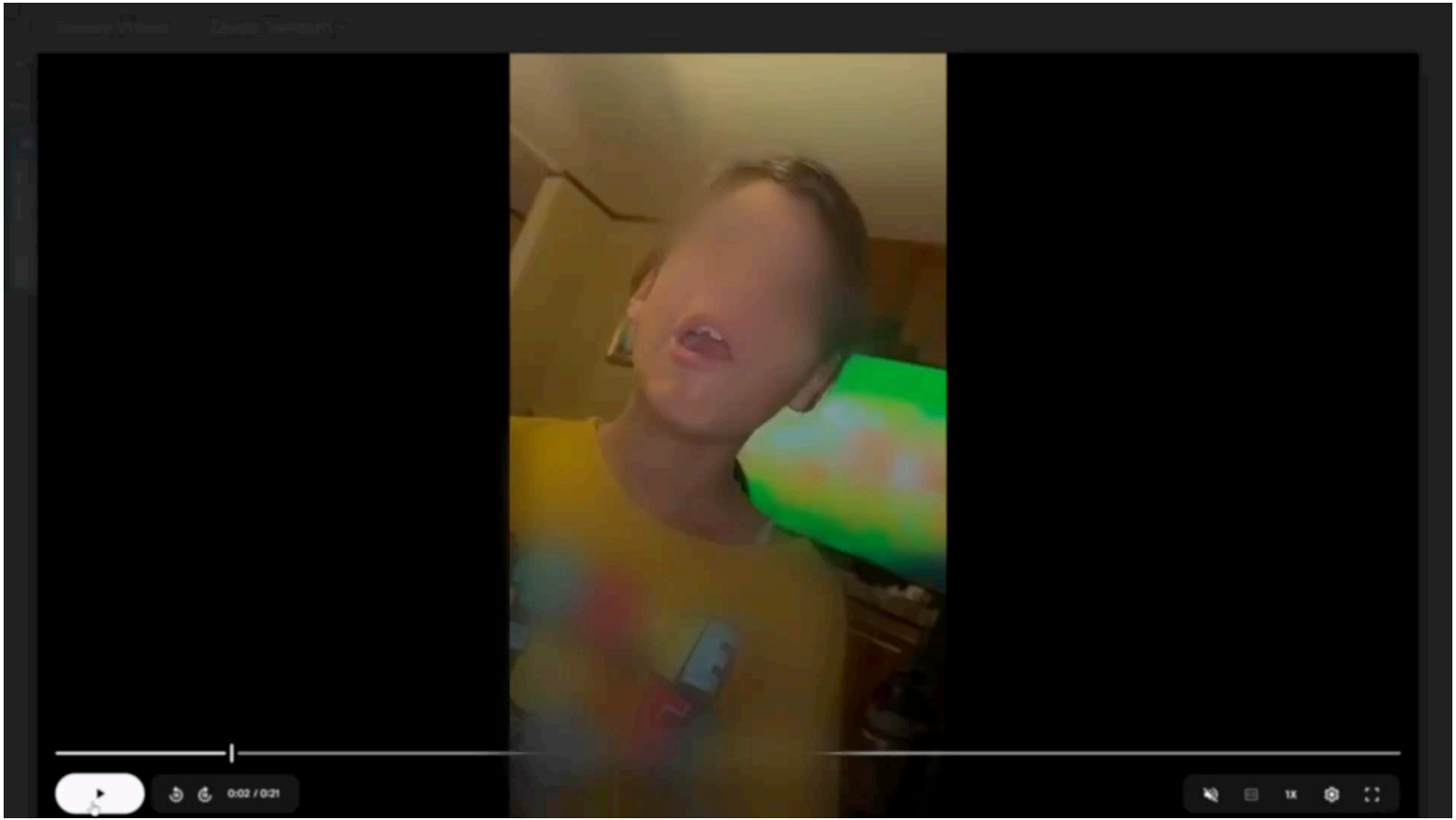
Case #4

- 5yo girl presents to your office with mother with complaint of multiple events per day of “staring off.”
- Mom thinks her daughter has ADHD, but no other significant history.
- Events consist of arrest of behavior and lip smacking lasting few seconds, then immediate return to baseline.
- Mother has a video to show you!



Childhood Absence Epilepsy

- Age of onset: 4-10yo
    - Caution if <4yo
- Development typically normal but may have learning difficulties or ADHD.
- Usually respond well to ASMs
    - Ethosuximide 1st line, then consider or valproic acid, levetiracetam, lamotrigine.
- Patient is started on ETH and does great! Two years pass, and mother sends you another video!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Idiopathic Generalized Epilepsy

- 40% may evolve into other idiopathic generalized epilepsy syndromes once into early adolescence.
- Red flags:
  - Generalized tonic-clonic (GTC) seizures prior to or during period of frequent absences.
  - Staring spells with >30-second duration or postictal confusion/fatigue.
  - Absences < daily in untreated patients.

Medication Pearls

Ethosuximide (Zarontin)

- 1st line for absence epilepsy; rarely used otherwise.
- Upset stomach is most common side effect but can also cause sleep disturbances and hyperactivity.

Valproic acid (Depakote)

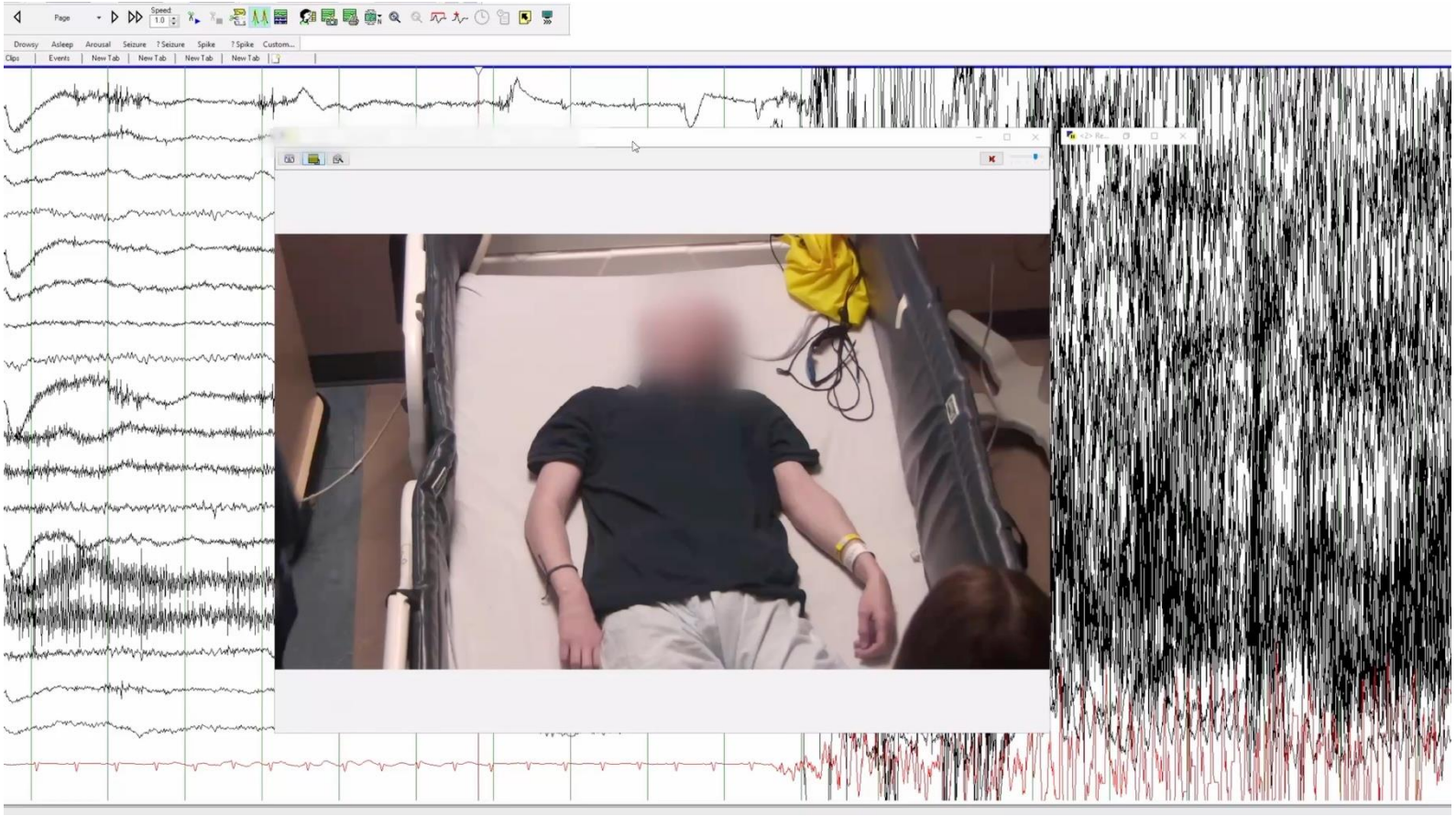
- Great broad spectrum; mood stabilizer.
- Weight gain, thrombocytopenia, teratogenic, narrow therapeutic window.

Lamotrigine (Lamictal)

- LONG titration to goal dosing due to risk of severe skin rash.
  - Rash can start on oral mucosa.
- Mood stabilizer (mild).
- Estrogen (birth control) can significantly lower lamotrigine levels.

Case #5

- 18yo man who presents to your office with concern for seizures.
- Flashing lights and florescent lights at school will make his whole body stiffen then convulse.
- He has fallen multiple times at school, including on the stairs, and now will only use the elevator.
- Family has a video of a typical event!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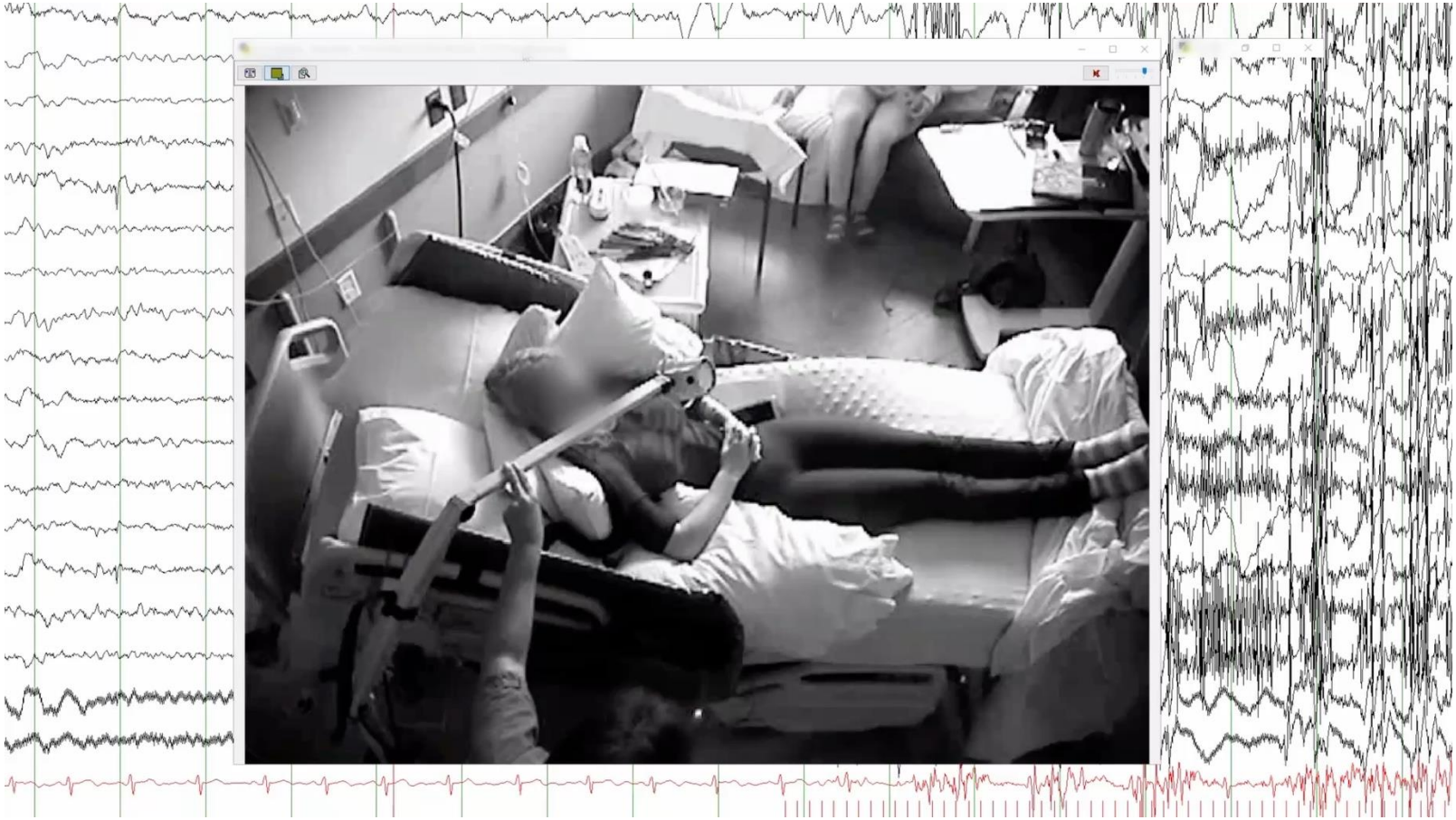
Psychogenic Nonepileptic Event (PNEE)

- Excellent remission rate (~80%) when appropriately managed.
- Semiologies range from unresponsiveness to violent convulsing (as in this case) and everything in between. Videos with or without EEG are very helpful.
- Management involves focused cognitive behavioral therapy.
- Dell Children's has a specialty clinic dedicated exclusively to helping patients with PNEE.

Case #6

- 17yo presented to your office with mother, who reported patient had two convulsive seizures, one in the car and one at home.
- Described as whole-body stiffening and shaking, drooling, and incontinence, all lasting about 2 minutes.
- Since then, in the morning she will notice a few single jerks of her upper extremities that cause her to drop things.
- Mother has a video of the seizure!



Juvenile Myoclonic Epilepsy

- Age of onset: 10-24 years.
- Development is usually normal.
- Myoclonic seizures, usually on awakening, are predominant seizure type.
- GTCs in >90%, which often evolve out of cluster of myoclonic seizures.
- Absence in 1/3, typically brief (3-8 seconds) and less than daily with variable impairment of awareness.
- Photic stimulation is a trigger: signs on EEG in 30-90%.
- Mostly very well managed on single broad-spectrum ASM: valproic acid, levetiracetam, lamotrigine (can worsen myoclonus), clobazam.

Antiseizure Medication Pearls

- Ask your patients with epilepsy and their caregivers about their ASMs.
    - Are they happy with the medication?
    - Are they having side effects?
    - Are they taking the medication regularly?

- Encourage your patients and caregivers to dialogue with their neurologist.
    - We want to help!

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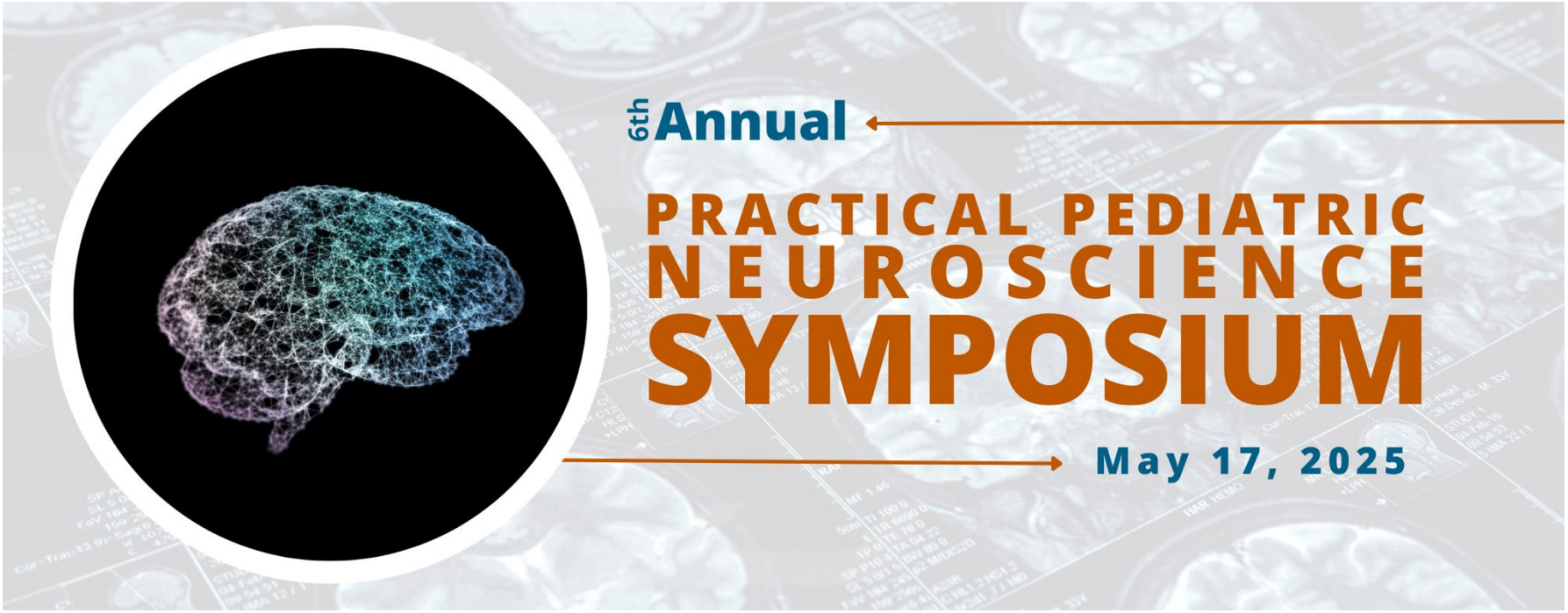

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