PAEDIATRIC SEIZURES

Facilitators Guide

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Author Peter Tormey Duration 1-2h Facilitator level Senior trainee/ANP and above Learner level Junior trainee/Staff nurse and Senior trainee/ANP Equipment required None

OUTLINE

- Basics (10mins)
- Main session: (3x 15 minute) case discussions covering the key points
- Advanced case (1x15 minute)
- Simulation (30-45mins)
- Quiz
- Take home learning points

PRE-READING FOR LEARNERS

Blog posts:

https://dontforgetthebubbles.com/first-afebrile-seizure/

https://dontforgetthebubbles.com/consept-eclipse-status-epilepticus/

www.stemlynsblog.org/jc-enter-sandman-which-agent-as-second-line-in-paediatric-status-epilepticus/

Podcasts:

www.paediatricemergencies.com/status-epilepticus/

https://pemplaybook.org/podcast/131/

https://broomedocs.com/2019/06/paediatric-status-epilepticus-debate/

BASICS

Α

Unprovoked seizures are common in children with around 8% having a seizure by 15 years of age ¹

В

Most seizures are brief, self-limiting and generally cease within 5 minutes ¹

С

Convulsive status epilepticus is the most common paediatric neurological emergency worldwide and the 2nd most common reason for PICU admission in the UK.²

D

A seizure is the clinical expression of abnormal, excessive, synchronous discharges of neurons residing primarily in the cerebral cortex³

Ε

The International League Against Epilepsy (ILAE) characterize seizure types as per the infographics below:





5

When a child presents to the ED with a seizure, there are two questions you must consider:

Was the seizure a primary event or secondary to something else?

 Seizures can be due to an underlying epilepsy or can be acute symptomatic seizures due to:

- Hyponatraemia
- Hypoglycaemia
- Hypocalcaemia
- High fever
- Toxin exposure
- Intracranial bleeding
- Meningitis

Was this really a seizure or should I consider other differentials?

Tonic clonic activity and incontinence are not specific for seizures so always consider differential diagnoses.

- Differential diagnosis of a seizure:1
- Vasovagal syncope
- Blue breath holding spell
- Reflex anoxic seizure
- Arrhythmia
- Non-epileptic paroxysmal event

Seek out clues in the history:

A sudden fright or minor trauma followed by the child turning pale and seizing is suggestive of a reflex anoxic event secondary to a vagal reflex. Hypoxia can induce a short tonic-clonic event that looks like a generalized tonic-clonic seizure but the child will recover quickly.

A history of a temper tantrum crescendo-ing into the child holding their breath, turning blue and then seizing might make you think of a breath holding attack. Again, this child will recover quickly.

Standing in a hot, stuffy room, feeling lightheaded with some visual changes and echoey hearing sounds vasovagal. Compare this to a child who describes palpitations or is exercising before the event; this child could have had an arrhythmia.

CASE 1

A 7 year old boy called Simon is brought to ED by his parents. At approximately 7am they were awoken by noises coming from his room. They ran in and noticed that the left side of his face was jerking and he was drooling and making gurgling sounds. He wasn't responding to them.

The movements stopped after 2 minutes. He was drowsy for a few minutes after and had difficulty talking and expressing himself for 15-20 minutes after. They also noticed there was a slight drooping on one side of his mouth for 15-20 minutes.

He has now fully recovered and is bright and alert in ED with GCS 15/15 and a normal neurological exam.

What are some of the key elements of Simon's past medical history that you must ascertain?

1-Any history of hypoxic injury at birth?
2-Did he have any delay in meeting his developmental milestones?
3-How does his school performance compare to that of his peers?
4-Is there any history of similar events? Or unusual behaviours or word-finding difficulties on waking from sleep?

The key here is to determine if Simon is an otherwise well child or if there are details in his medical history, such as developmental delay, that may make him more prone to developing epilepsy

It is also important to determine if he perhaps has had more subtle seizures in the past that may have been missed

How would you classify his seizure?

This is an opportunity to look at the International League Against Epilepsy infographic.

Simon has had a focal motor seizure with impaired awareness.

Are there clues in the history as to what specific seizure disorder he may have?

Specific seizure disorder: Simon's seizure would be most in keeping with a clinical diagnosis of benign childhood epilepsy with centrotemporal spikes **(BCETS)** also known as **benign rolandic epilepsy.**

BCETS usually presents in **early school age** children with **normal development**. The most common seizure type is a **focal motor** seizure involving the face. There may or may not be impaired awareness. They can also be associated with facial numbness, hypersalivation, drooling, dysphasia and speech arrest. Motor activity in the upper, but not lower, limbs is common. They may also progress to a generalized tonic-clonic seizure.3 Approximately 75% of seizures occur **at night or on awakening** and, therefore, can be easily missed. Patients may have a **post-ictal paresis**, often of one side of the face which can be concerning for a cerebrovascular accident.

Would you perform any investigations at this point?

A blood glucose should be checked.

Electrolytes are often checked with a first seizure but their utility decreases with patient age and degree of recovery. ⁵

As this history is strongly in keeping with a diagnosis of BCETS, an EEG is not strictly necessary to confirm the diagnosis, however, your local guideline for first seizure management should be followed.

There is no indication for neuroimaging at present.

Does he need to be admitted? Does he need treatment? What follow up will you arrange?

Patients generally do not need to be admitted after a first seizure with no red flags: 1

• Seizure related to head injury

- Developmental delay or regression
- Headache prior to seizure
- Bleeding disorder or on anticoagulant medication
- Drug or alcohol use
- Focal neurological signs or incomplete recovery
- Seizure > 5 minutes

• Social concerns e.g parental coping mechanisms or concerns over parental ability to recognize and seek medical attention if another seizure were to occur

Patients with an uncomplicated first seizure generally do not need to be commenced on treatment. BCETS in particular generally has a benign course and rarely requires treatment.

All children who have a first seizure episode should be referred for paediatric follow up. This may be General Paediatric or Paediatric Neurology follow up and local referral pathways should be consulted.

The International League Against Epilepsy have a useful infographic for managing a first seizure:



Clinical variables associated with increased risk of seizure recurrence:

- a prior brain injury
- epileptiform activity on EEG
- abnormal brain imaging (CT/MR1)
- a nocturnal seizure



Antiepileptic drug (AED) treatment

Clinicians recommend that first seizure treatment decisions should be individualized according to :



Image 3. ILAE inforgraphic for first seizure management⁴

For more information on managing a 1st afebrile seizure see: https://dontforgetthebubbles.com/first-afebrile-seizure/

CASE SCENARIO 2: PANAYIOTOPOULOUS SYNDROME

Emily is a 4 year old girl brought to ED with episodes of disturbed sleep for the last 3 weeks. This is her 4th visit to ED. She was previously diagnosed with "night terrors" and reassured. Her mum is concerned because the episodes are now occurring each night, having previously been 1-2 per week.

Her mum has videos of the episodes, which she shows you. The events usually occur shortly after going asleep. In the videos Emily wakes from sleep, looks terrified and stares straight ahead. The episodes go on for 2-3 minutes. She usually vomits or retches towards the end of the episode. She goes back to sleep after. She is well during the day.

Her development is normal and she has no other medical history.

What could be going on here?

These episodes sound unusual and their frequency and severity seems more pronounced that what could be put down to normal variance in sleep pattern and arousal. Emily's symptoms are not likely to be simple night terrors.

Seizures commonly occur in sleep and as a result can be missed or present subtly or without characteristic features.

What interesting details in the history might lead you towards a specific diagnosis?

There are several features in the history that would suggest **Panayiotopoulous Syndrome** (PS).

PS is a focal epilepsy that occurs in children aged 1-14 years with a mean age of 5 years. The seizures are usually **nocturnal.**

It is thought PS accounts for 6% of children with epilepsy.7

There is a strong association with **vomiting** (70-85%) of patients. **Visual symptoms** are also closely related, given the seizures originate in the occipital

lobe. Autonomic features can also be seen: pallor, tachycardia, miosis, coughing and hypersalivation.⁷

They may also have head or eye deviation and focal or generalized clonic activity.

The diagnosis of PS is often delayed due to misdiagnosis with other causes of vomiting and autonomic manifestatons e.g encephalitis, migraine, syncope or gastroenteritis.8

What could help differentiate between epileptic and non-epileptic events in this case?

PS could easily be clinically misdiagnosed as night terrors. Night terrors are dramatic awakenings that usually happen during the first few hours of sleep. They share several characteristics with PS but there are also some subtle differences highlighted in the table below:

Clinical Feature	PS	Night Terrors
Usual duration 5-10min	+	+
Occur during the first few hours of sleep	+	+
Autonomic Symptoms e.g tachycardia,	+ +	+
tachypnea, sweating	+	
Impaired awareness	+	+
Child looks scared	+ +	+
Starring		+
Running or walking around during	-	++
episode		
Screaming	-	++
Vomiting	+ +	-
Thrashing of arms and legs	-	++

Table 1. Clinical characteristics of PS and night terrors

It is not unreasonable to clinically diagnose night terrors if they present with characteristic events, more in keeping with night terrors than PS. However, if there are unusual features, such as vomiting, or exaggerated autonomic symptoms, or in a child who represents, then an alternative diagnosis should be considered.

An inter-ictal EEG will usually be diagnostic in PS with occipital spikes, which are enhanced in sleep, the characteristic feature. In a child with unusual events occurring in sleep and a normal EEG, a video telemetry EEG may be useful to try and capture and characterise the events and outrule seizures as a possibility.

What is the prognosis for these patients?

PS usually has a benign course with spontaneous remission commonly occurring within 2-3 years of onset.

Seizures are generally infrequent but oxcarbazepine may be required to reduce seizure frequency.

ADVANCED CASE SCENARIO 1: STATUS EPILEPTICUS

Emma is a 3year old girl with a background of refractory epilepsy and developmental delay. Her current medications include levetiracetam, sodium valproate, clobazam and lamotrigine.

She is PEG fed but has been vomiting up her feeds for the last 2 days and mum is unsure if her medications have been staying down.

She normally has up to 20 short seizures per day at home, but this has been increasing in the last 2 days.

You get a pre-alert from the ambulance service: Emma has been having a generalized tonic clonic seizure for 15 minutes. Her mum gave her bucca midazolam at 5 minutes but it has not had any effect.

The ambulance crew ask you can they repeat the dose of buccal midazolam?

There is a risk of respiratory depression with any benzodiazepine.

A Cochrane review9 in 2018 found that 25/346 (7.2%) patients treated with buccal midazolam experienced respiratory depression. There was no statistically

significant difference in risk of respiratory depression between buccal midazolam and other benzodiazepines, administered via various routes.

The drug information leaflet or Summary of Product Characteristics (SPC) for Buccolam[®] and Epistatus[®] recommend that only a single dose be administered at home by a caregiver and that additional doses should only be administered after seeking medical advice and, preferably, under medical supervision.

In this case, it would be reasonable to advise a second dose of bucca midazolam, presuming the paramedics had the necessary equipment and skillset to manage any respiratory depression that may occur.

Factors that may influence your decision are: the ETA of the ambulance and if the child has a history of respiratory depression with benzodiazepines.

Emma arrives in resus with the seizure ongoing. What is your management plan?

She should be managed as per the APLS guideline (please note this is the Australian APLS guideline and has been updated to include the use of levetiracetam as a second line agent. This has not yet been included in the UK APLS guideline, see discussion below):



Image 4. Australian APLS guideline for management of status epilepticus

Emma has had two doses of benzodiazepines. What would be your next line agent? Who else should you be calling at this stage?

At this point you should be informing PICU about the patient and your PEM consultant if you haven't done so already.

The CONCEPT10 and ECLIPSE2 trials were published concurrently in May 2019.

These two studies looked at whether levetiracetam is non-inferior to phenytoin as a second line treatment in the management of convulsive status epilepticus in children.

This question was posed as phenytoin is linked to many adverse events including liver damage, Steven-Johnson syndrome, extravasation and reports of death due to dosing errors. As a result, and because of its biopharmacology, it is a resource-intensive drug to make up in an emergency.

Levetiracetam can be given over 5 minutes (phenytoin takes 20 minutes to infuse), is more compatible with IV fluids, has less drug interactions, and has a lower risk of adverse events.

The infographic below provides a nice summary:

SEIZING THE TRUTH?

PREDICT

EcLiPSE PERUKI

WHAT SHOULD THE SECOND LINE TREATMENT FOR STATUS EPILEPTICUS BE?

PHENYTOIN LEVETIRACETAM 20mg/kg over 20 minutes 40mg/kg_over 5 minutes 30 EDs 13 EDs US + N3 mo - 16 yrs 6 mo - 18 yrs n= 134 PHENYTOIN n= 114 LEVETIRACETAM n= 152 n= 119 SEIZURE CESSATION TIME FROM 1 **5 MINUTES AFTER** PRIMARY RANDOMISATION TO END OF CONVULSIONS INFUSION END OUTCOME **37-40%** IF THERE WAS ONGOING SEIZURE POST, THE OTHER DRUG WAS GIVEN AS THIRD LINE RESULTS SEIZURE CESSATION **MEDIAN TIME TO 5 MIN POST SEIZURE STOP PHENYTOIN 60%** PHENYTOIN 45 MIN **LEVETIRACETAM 35 MIN LEVETIRACETAM 50%** CONCLUSION **LEVETIRACETAM NO SIGNIFICANT NOT SUPERIOR** DIFFERENCE

READ THE FULL DFTB POST ABOUT THIS AT HTTP://DOI.ORG/10.31440/DFTB.18696 DONTFORGETTHEBUBBLES.COM @GRACIE_LEO Image 5. Infographic summarizing the ConSEPT and EcLiPSE trials

You can find a more detailed summary at: https://dontforgetthebubbles.com/ consept-eclipse-status-epilepticus/

It's important to note that the primary outcomes of the two studies were different:

ConSEPT – The primary outcome was seizure cessation 5 minutes after the drug infusion and where possible the seizure cessation was verified independently via a video recording to reduce observer bias between the two groups.

EcLiPSE - In a key difference to the ConSEPT study the primary outco was time "from randomisation to cessation of all visible signs of convulsive activity, defined as cessation of all continuous rhythmic clonic activity, as judged by the treating clinician". As per the inclusion criteria this a very real world pragmatic approach.

The two studies concluded:

ConSEPT – Levetiracetam is not superior to phenytoin as a second line agent for convulsive status epilepticus **EcLiPSE** – There is no significant difference between phenytoin and levetiracetam in the second-line treatment of paediatric convulsive status epilepticus for any outcome, including time to seizure cessation Here is a section of the commentary from the post:

"While there were differences between the study designs, the primary outcome measure of timing being the largest, the fact that both studies found no

difference probably means head-tohead there is little difference.

The nature of the statistical analysis means that both groups rightly point out that in their cohorts levetiracetam wasn't superior in outcomes to phenytoin. A future pooled analysis could still demonstrate a difference, but it seems unlikely that a critical difference will

be seen (especially for the safety element).

Given the wealth of evidence on the side effects of phenytoin it is surprising the incident rates were relatively low. Whether in study conditions more care was taken with drawing up and delivering the drug or that previous safety

reviews were heterogenous in their inclusion criteria is difficult to know. However, the time to draw up phenytoin, and the background concerns on its potential harm, will lead some to suggest that the switch to levetiracetam is a logical one, regardless of its effectiveness against phenytoin.

The challenge faced by many units is a capacity for PICU beds. Because phenytoin is given over 20 minutes there is time to prepare for airway/ anaesthetic intervention if it is unsuccessful in terminating the seizure. The use of levetiracetam may cause some to wonder if they should then try phenytoin either as a stop gap to bed availability or because the time in status now seems 'shorter' than normal. These are not statistical issues, these are pragmatic clinical conundrums.

The absence of a clear winner will further fuel this debate meaning it is unlikely in the immediate future we are going to see a change from the ALSG or similar organisations. However, local units may decide, in the clear absence of harm from levetiracetam, that it is a drug they should be adding into their treatment protocols."



You decide to suggest these papers for your department's next journal club and to discuss what effect they will have on your department's practice. One issue you foresee is that a lot of the patients you see are already on maintenance levetiracetam.

Does this preclude children on maintenance levetiracetam from receiving IV levetiracetam in status epilepticus, as is the case with the use of phenytoin in patients who take it as maintenance treatment?

The EcLiPSE trial2 did not report any increase in adverse events in children who were on maintenance leveltiracetam and received a loading dose of IV levetiracetam. The ConSEPT trial excluded all patients who were on maintenance levetiracetam and phenytoin.

The use of phenytoin in status epilepticus in patients who are on maintenance phenytoin is avoided due to its potential cardiovascular side effects. As levetiracetam does not share these side effects and is generally safe and well tolerated it is reasonable to use it in children who are already on maintenance therapy.

Emma's seizure terminated with the second line agent and she was admitted under neurology for IV fluids and ongoing management of her seizures until she could tolerated her medications by PEG again. In this case her status epilepticus was likely due to her vomiting up her medications.

Had Emma's seizure not stopped after the loading dose of phenytoin, what would your next steps be?

The current APLS guidance in the UK would be to proceed with RSI. As we have discussed above, the Australian APLS guidelines have changed, in view of the results of the ConSEPT and EcLiPSE, to include the use of an additional second line agent prior to proceeding to RSI. As reported in the ConSEPT trial, treatment with one drug and then the other reduced the failure rate by more than 50% at the expense of only an additional 10 minutes.

For further discussions on advanced seizure management and RSI, the following podcast is recommended:

https://broomedocs.com/2019/06/paediatric-status-epilepticus-debate/

ADVANCED CASE SCENARIO 2: SEIZURES SECONDARY TO BRUGADA SYNDROME

Caroline is a 13 year old girl who present to ED with a first seizure. Her parents describe a generalized tonic clonic seizure that lasted 2-3 minutes.

She is an otherwise well girl who is doing well in school. The only concern in her past medical history is that she has been having frequent syncopal episodes for the last 12 months. She has been seen by her GP for this who reassured her that syncopal events were common in her age group and advised her to drink plenty of fluids and try and avoid triggers.

Her neurological exam is normal.

How would you proceed?

A blood glucose should be checked. If she has returned to her baseline and there were no red flags with regard to the seizure it would be reasonable to arrange outpatient follow up as per departmental protocol and advise her parents what to do if she should have further seizures.

Are there any investigations you could perform in the department to investigate the syncopal episodes she reports?

An ECG and a lying-standing blood pressure should be performed.

Is there any link between syncope or arrhythmogenic events and seizures?

Seizures may be triggered by cerebral hypoperfusion due to an arrhythmic event. They can often be treated as a primary seizure and the underlying cardiac abnormality may be missed. 11 Long QT syndrome in particular can present with seizures and almost half of affected patients are initially misdiagnosed and treated for epilepsy before the correct diagnosis is made.¹¹

Seizures can also be seen as a primary neurological abnormality, related to the cardiac abnormality. Brugada Syndrome is an autosomal dominant condition characterized by ECG alterations and a predisposition to tachyarrhythmias and sudden death. 12 It is caused by a mutation in the genes SCNA5 and SCN1A.

SCN5A codes for the alpha subunit of the voltage-gated sodium channel. As the condition is a channelopathy it can also be associated with epileptic seizures with the channelopathy affecting neuronal pathways.

Caroline has an ECG performed which shows changes consistent with Type 1 Brugada Syndrome.



Image 6. ECG findings consistent with Brugada Syndrome

There is coved ST segment elevation in V1 and V2 with a negative T wave. This is the only ECG abnormality that is potentially diagnostic and is often referred to as Brugada sign.

For an approach to the paediatric ECG have a look at the following DFTB post: https://dontforgetthebubbles.com/approaching-the-paediatric-ecg/ For further reading on the specific ECG findings in Brugada Syndrome, please see:

https://litfl.com/brugada-syndrome-ecg-library/

Caroline is admitted for further cardiac investigation and is scheduled for an ICD insertion. She also has an EEG, diagnostic for frontal lobe epilepsy, which is linked to ion channel abnormalities.

SIMULATION

http://www.oxforddeanery.nhs.uk/pdf/Paediatrics_8.pdf

QUIZ

Question 1.

Which symptom is more commonly seen with Panayiotopoulos Syndrome than night terrors?

Α	В	С	D	E
Starring	Terrified	Vomiting	Thrashing of arms and	Tachypnoea
			legs	

70-85% of seizures in PS are associated with vomiting. Vomiting is not usually described in night terrors. The diagnosis of night terrors should be carefully applied to children having events disturbing their sleep that have a strong association with vomiting.

Question 2.

Which of the following are side effects of phenytoin but not levetiracetam?

A D
 Mood disturbance Gingival hypertrophy
 B E
 Cardiovascular toxicity Stevens Johnson syndrome
 C

Purple glove syndrome

Although levetiracetam and phenytoin have several common side effects, cardiovascular toxicity, purple glove syndrome and gingival hypertrophy are more

specific to phenytoin and are not generally seen with levetiracetam. Mood disturbance is one of the most common side effects of levetiracetam. Stevens Johnson syndrome is also reported with levetiracetam.

Question 3.

Which of the following ECG findings are seen in Brugada Syndrome:

A

Coved ST segment elevation in V1-3, >2mm

B

Prolonged PR interval

С

Negative T wave

D

Saddleback ST elevation, >2mm

E

LVH voltage criteria

Brugada Type 1 has coved ST segment elevation in V1-3, >2mm, followed by a negative T wave. This is often referred to as the Brugada sign. Brugada Type 2 has & >2mm of saddleback-shaped ST elevation Brugada Type 3 can have the morphology of type 1 or 2 but with & <2mm ST segment elevation Prolonged PR interval and LVH voltage criteria are not characteristic features of

Brugada syndrome

Take Home Messages

- Seizures are common in sleep and may present subtly- be wary of unusual events occurring around sleep and have a low threshold to investigate them for seizures
- 2 Make sure you have satisfied yourself there are no seizure red flags prior to discharging patients with a first afebrile seizure
- 3 Management of status epilepticus should proceed according to APLS and local guidelines
- 4 Levetiracetam may become a common choice second line agent for status epilepticus but for now it is advisable to continue to use phenytoin if you and your department have more familiarity with it.
- 5 It is important to identify and treat any precipitating cause for status epilepticus
- An ECG should be performed in all patients presenting with seizures

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