LRI Children's Hospital

Afebrile seizure: newly diagnosed epilepsy

Staff relevant to:	Medical & Nursing staff
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1. Introduction & Scope

Seizure is a common presentation. At least 10% of the UK population will have at least one seizure at some point in their life. A seizure may be epileptic or non-epileptic. An epileptic seizure may or may not be secondary to an acute neurological or any other generalised illness.

A first seizure associated with an acute illness is unlikely to recur (3-10% recurrence). Some children after a first epileptic seizure will go on to have further seizure and can be diagnosed with Epilepsy.

Epilepsy is a common condition, which can be associated with significant morbidity or mortality due to complications e.g. SUDEP (Sudden unexpected death in epilepsy). Many different types of epilepsy and epilepsy syndromes exist, varying in terms of presentation, management and prognosis.

This guidelines aims to provide a simplified approach for patients presenting with afebrile +/- recurrent afebrile seizures. This helps in establishing the diagnosis and management of a patient with newly diagnosed epilepsy.

This guideline is intended for use by Medical and Nursing staff working within UHL Children's Hospital caring for children who present with recurrent afebrile seizures.

There is a NICE guideline available for professionals treating children following a possible afebrile seizure NICE guidance 217. This guideline is an adapted version of the NICE guidelines and the locally agreed protocol to aid management of first afebrile seizure (s).

For children admitted for inpatient assessment, follow-up to be discussed with the lead paediatric consultant.

For children assessed in the Emergency department with a suspected afebrile seizure, referral to General Paediatric outpatient to begin with, should be made. If the child or young person is already known to a neuro-disability consultant, please also inform them as soon as, review with them may be more appropriate.

Related documents:

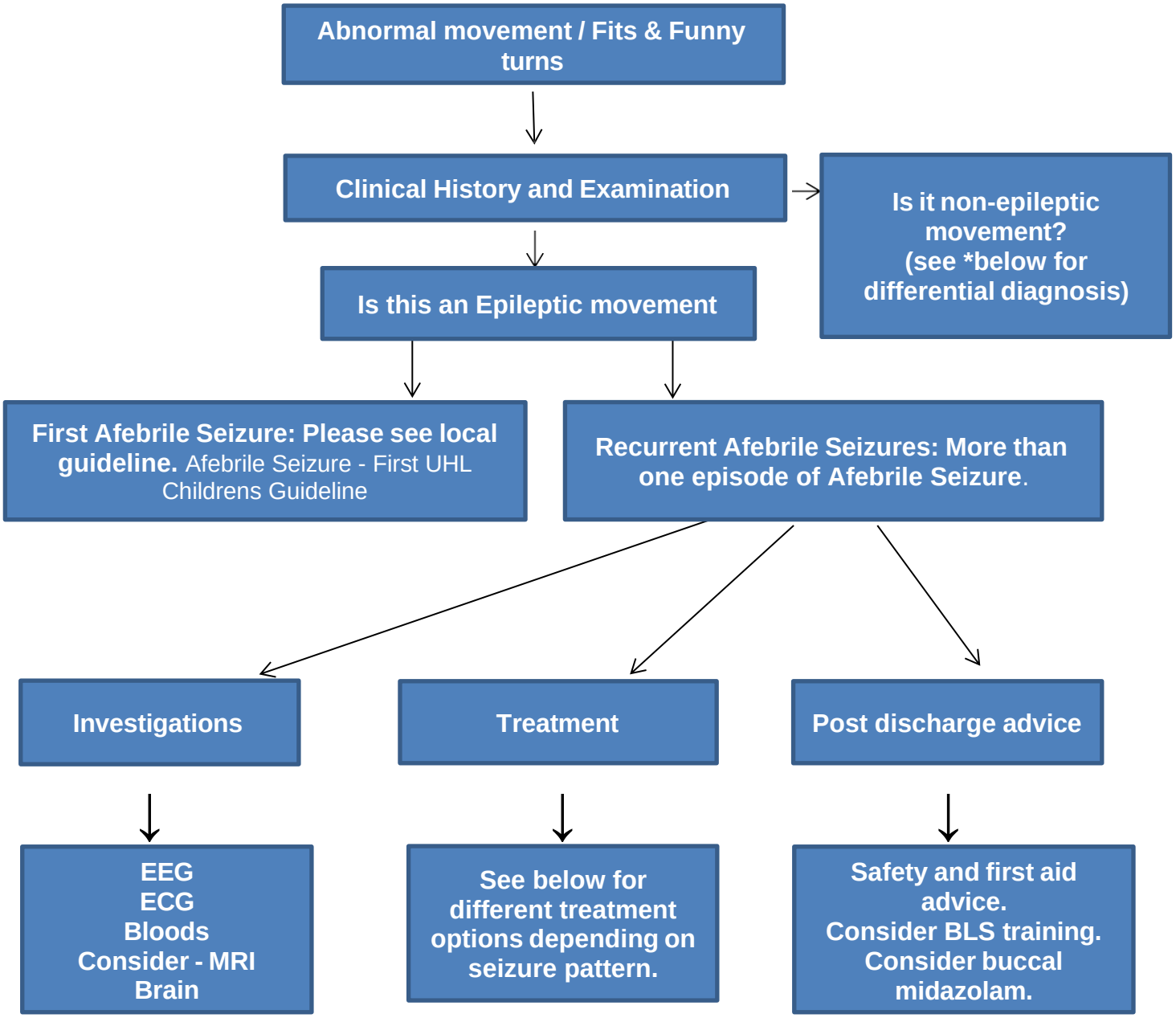
- **Febrile Convulsions UHL Childrens Guideline**
- **Seizure Management UHL Childrens Hospital Guideline**
- **Afebrile Seizure - First UHL Childrens Guideline**
- **Status Epilepticus UHL Childrens Hospital Guideline**

Definition

An epileptic seizure is defined as manifestation(s) of epileptic (excessive, abnormal and/or hypersynchronous) activity of neurons in the brain.
ILAE (International league against epilepsy) has proposed the diagnosis of epilepsy following:

- At least two unprovoked seizures occurring >24 hours apart;
- Or a single seizure when assessments suggests a high probability of further events
- Diagnosis of an epilepsy syndrome.
- Seizure not related to temperature / illness or any other trigger

2. Management flow chart



***Common differential diagnosis of non-epileptic seizure**

1. Febrile convulsion
2. Cardiac Arrhythmia
3. Vasovagal syncope
4. Breath holding attack
5. Reflex anoxic seizures
6. Seizures secondary to metabolic or electrolyte imbalance
7. Gastro-oesophageal reflux in infants
8. Non-epileptic attack disorder

Tics or movement disorder can also be differential diagnosis of focal motor seizures.

3. Initial management

A continuing convulsive seizure with loss of consciousness is a paediatric emergency. Ensure first aid/ ABC stabilisation including a normal blood sugar.

Refer to Status Epilepticus UHL Childrens Hospital Guideline

Children with an existing diagnosis of epilepsies, suspected epilepsy or other paroxysmal disorder should be managed by the epilepsies guideline or their individual care plan.

4. Clinical Assessment & diagnosis

- Take a detailed history from the CYP after first suspected seizure. Eyewitness's account and video clip of the seizure should be taken in account.
- Carry out a physical examination.
- Perform 12 lead ECG to help identify cardiac related conditions that could mimic epileptic seizure.
- Treatable conditions e.g., pyrexia, sepsis or hypoglycaemia should be ruled out.
- Consider neuroimaging with MRI head or CT head if either encephalopathy or focal neurology is present.

Emphasis on clear & detailed documentation of seizure is important. Document who the history is from and who witnessed the seizure, along with details of pre-ictal, ictal and post-ictal phase, including any focal neurology or deficits, which are important in guiding the diagnosis and ongoing management.

5. Investigations

Routine investigations are not always indicated in a child over 18 months with an afebrile seizure, who do not fulfill the criteria for admission.

- Glucose

A finger prick blood glucose level should be performed if a child is still seizing or not fully alert.

- ECG

A 12 ECG should be performed, with recorded calculation of QTc. Prolonged QTc is a potential cause for recurrent afebrile seizure. Children with arrythmias or other causes of syncope can present with convulsive syncopal seizures that mimic epileptic seizure.

- Blood

No routine blood test is required.
U&E, Ca, Mg, FBC and urine toxicology can be considered if child in very young and teenagers or else suggested by history.

- EEG

All children with **recurrent** suspected epileptic seizure should have an EEG.
The EEG should not be used to exclude a diagnosis of epilepsy in a child, young person or adult in whom the clinical presentation supports a diagnosis of a non-epileptic event. The EEG should not be used in isolation to make a diagnosis.

- CT/ MRI Brain

NICE (2022 March) recommends MRI to be the preferred imaging investigation of choice in children, young people and adults with epilepsy. If required, it should be done within 6 weeks of presentation.
Not every child with epilepsy requires MRI investigation but MRI should be offered to children:

1. who develop recurrent epileptic seizure before the age of 2 years
2. who have any suggestion of a focal onset on history, examination or EEG (unless clear evidence of benign focal epilepsy)
3. Children in whom seizures continue in spite of first-line medication
4. Suspected neurocutaneous syndrome

Typical MRI Contraindications
- **Metallic Shunts, clips, pumps, valves and stents**
- **Pacemakers & defibrillators**

Special considerations (Possible but need discussion with MRI dept)
- **Teenager with possibility of pregnancy**
- **Neurostimulator e.g. vagal nerve stimulator**
- **Cochlear implant**
- **Dental braces**
- **Renal impairment and IV contrast contraindicated**

6. Treatment, Information and Support

Epilepsy is a treatable condition and around 70% of people with epilepsy will become seizure free with appropriate medication. Anti-epileptic drugs (AED) are mainstay of treatment in epilepsy.
Anti-epileptic drugs are chosen based on the seizure type and epileptic syndrome. Before starting medication, discussion with the patient on treatment strategy as per the epilepsy type, personal preference and individual circumstances is important.
The updated guidance stresses the importance of taking fewest medicines possible to optimize the seizure control.
Specific recommendations for choice of AED, support and monitoring of AED is made for girls of child bearing age.

NICE guidelines on shared decision making (https://www.nice.org.uk/guidance/ng197) is helpful in discussing the diagnosis and management with the child, young person and the family (currently under review with regards to new patient safety alert for Sodium Valproate medication).

7. When to start anti-seizure drug (AED) –

Use a single AED (monotherapy) where possible. If first line is unsuccessful and diagnosis remains confirmed, try monotherapy with 2nd or 3rd line, using caution over changeover period.

- Start treatment with an AED once diagnosis of epilepsy is confirmed.
- Consider starting treatment after a first unprovoked seizure if any of the following apply:
    1. Clinical examination identifies signs of neurological deficit.
    2. The EEG confirms unequivocal epileptic activity.
    3. Brain imaging shows a structural abnormality.
    4. If risk of further seizures and the person or their family, consider the risk unacceptable.

Table 1- AED options by seizure type

For Sodium Valproate medication- see national patient safety alert (November -2023) - mentioned in this guideline

Seizure type	First-line AEDs- Monotherapy	Second-line AED's - monotherapy	Third-line AED as Add on therapy
Generalised tonic–clonic	Lamotrigine or Levetiracetam	Lamotrigine Levetiracetam	If monotherapy is unsuccessful: Add on options: Clobazam Lamotrigine Levetiracetam Perampanel Topiramate
Tonic or atonic	Lamotrigine	Lamotrigine Clobazam Rufinamide Topiramate	Ketogenic diet as add on tx
Absence	Ethosuximide	Lamotrigine Levetiracetam	
Focal with or without bilateral tonic-clonic	Levetiracetam Lamotrigine	Carbamazepine Oxcarbazepine Zonisamide	Carbamazepine Lacosamide Topiramate
Myoclonic	Levetiracetam	Topiramate Levetiracetam Lamotrigine Clobazam Zonisamide	

Table 2- AED options by epilepsy syndrome

Epilepsy syndrome	First-line AEDs	Adjunctive AEDs
Dravet Syndrome	**To discuss with paediatric neurology team**	Triple therapy by adding Clobazam Stiripentol
Self-limited epilepsy with centrotemporal spikes	**Medications are not always indicated** **Consider-** Lamotrigine Levetiracetam	Carbamazepine Oxcarbazepine Zonisamide
Juvenile myoclonic epilepsy	Lamotrigine Levetiracetam	Levetiracetam Lamotrigine
Infantile spasms not due to tuberous sclerosis	High dose prednisolone and vigabatrin as combined therapy. Consider Vigabatrin alone in children at high risk of steroid related side effect. Discuss with, or refer to, a tertiary pediatric epilepsy specialist	Levetiracetam Topiramate Ketogenic diet
Infantile spasms due to tuberous sclerosis	Vigabatrin or steroid (prednisolone) or combined therapy Discuss with, or refer to, a tertiary paediatric epilepsy specialist	

MHRA advice on Valproate- Recent- Nov 2023-

https://www.gov.uk/drug-device-alerts/national-patient-safety-alert-valproate-organisations-to-prepare-for-new-regulatory-measures-for-oversight-of-prescribing-to-new-patients-and-existing-female-patients-natpsa-slash-2023-slash-013-slash-mhra

Based on current information and alerts, *Sodium Valproate should not be started even in males also* and seek specialist advice if considering Sodium Valproate in age <55 years.

The regulatory change in January 2024, for oral valproate medicines, means that:

A. Valproate must not be started in new patients (male or female) younger than 55 years, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the

reproductive risks do not apply.

B. At their next annual specialist review, women of childbearing potential and girls should be reviewed using a revised valproate Risk Acknowledgement Form, which will include the need for a second specialist signature if the patient is to continue with valproate and subsequent annual reviews with one specialist unless the patient's situation changes

MHRA previous alert-

In April 2018, revised again in January 2021- warnings were added that valproate treatment must not be used in girls and women including in young girls below the age of puberty, unless alternative treatments are not suitable and unless the conditions of the **pregnancy prevention programme (PPP)** are met.

The Pregnancy Prevention Program is a system of ensuring all female patients taking valproate medicines: (1. have been told and understand the risks of use in pregnancy and have signed a Risk Acknowledgement Form, 2. are on highly effective contraception if necessary and 3.see their specialist at least every year) Medicines containing valproate taken in pregnancy can cause malformations in 10% of babies and neurodevelopmental disorders in 30–40% of children after birth.

https://www.gov.uk/drug-safety-update/valproate-medicines-epilim-depakote-contraindicated-in-women-and-girls-of-childbearing-potential-unless-conditions-of-pregnancy-prevention-programme-are-met

Liver dysfunction (including fatal hepatic failure) has occurred in association with valproate (especially in children under 3 years and in those with metabolic or degenerative disorders, organic brain disease or severe seizure disorders associated with mental retardation) usually in first 6 months and usually involving multiple antiepileptic therapies.

In myoclonic seizures, carbamazepine can exacerbate seizures.

Although Levetiracetam is mentioned as an adjunctive therapy for focal seizure in BNFC, it can be used as monotherapy if Carbamazepine and Lamotrigine are unsuitable or not tolerated as per NICE guidance. Same dose of Levetiracetam should be used (as mentioned as adjunctive therapy) according to BNFC as discussed with Paediatric Neurology team at LRI. Similarly, Levetiracetam can be used as monotherapy in benign epilepsy with centrotemporal spikes, myoclonic and in juvenile myoclonic epilepsy.

All pregnant females with epilepsy, whether taking medication or not, should be encouraged to notify the UK Epilepsy and Pregnancy register (available at*: https://www.epilepsyandpregnancy.co.uk).*

8. Referral to neurology team

Referral to tertiary Paediatric neurology needs to be consultant to consultant referral. The following are the criteria for referral to Tertiary Paediatric neurology service

1. Movement disorders
2. Already diagnosed complex Epilepsy syndromes
3. Suspected Epileptic seizures in children less than two years and/or specific Epilepsy syndrome
4. Children with diagnosis of Epilepsy on **OR** tried two or more different anti-epileptic drugs

9. Follow up

Patients with well-controlled Epilepsy stable on single AED (Anti-Epileptic Drug) will be followed up by the general Pediatrician.

Patients with poorly controlled Epilepsy (on two different AED) or patients on single AED needing more input in view of more seizures will be seen by either Pediatrician with interest in Epilepsy or Paediatric neurologist based on the complexity.

Referral to Epilepsy Specialist Nurse for first aid/safety advice, life style advice and rescue medication (midazolam)/BLS (in case of prolong seizures) training.

10. Reducing the risk of Epilepsy related death, including sudden unexpected death in epilepsy (SUDEP)

Discuss SUDEP risk with the family and CYP early, preferably at the time of the diagnosis, to explore and agree ways to reduce the risk.
(https://sudep.org/sudden-unexpected-death-epilepsy-sudep)

11. Checklist of issues that can be covered during consultations with patient/family:

Epilepsy in general https://www.epilepsy.org.uk/info/about https://www.epilepsy.org.uk/info/children-young-adults/children	
RCPCH document- Safety-netting information following a first seizure without a fever in children and young people https://www.rcpch.ac.uk/resources/safety-netting-information-following-first-seizure-without-fever-children-young-people	
Medications/management	
Sodium Valproate medication? Review new MHRA regulation and national patient safety alert Annual Risk Acknowledgement Form Review Pregnancy Prevention Programme (PPP) Patient guide	
Side effect of medications https://www.medicinesforchildren.org.uk/medicines/	

Monitoring – e.g. FBC / LFT/ Bone profile/ Vit D	
Discuss supply of medications / on-going prescriptions- Hospital / GP	
Risk management e.g. swimming, climbing heights https://www.epilepsy.org.uk/info/daily-life/safety	
First aid advice https://www.epilepsy.org.uk/info/firstaid/what-to-do	
For prolonged seizures – BLS & midazolam training, midazolam before discharge	
Lifestyle issues: smoking, alcohol consumption, driving, career choices	
Prognosis	
SUDEP (Sudden unexpected death in epilepsy) https://sudep.org/sudden-unexpected-death-epilepsy-sudep	
Link to Support group or charity organisations e.g. Epilepsy Society/ Epilepsy Action / Epilepsy Research UK https://www.epilepsysociety.org.uk/ https://sudep.org/ https://www.epilepsy.org.uk/	

Education & training

None

Monitoring compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Children and young people who meet the criteria for neuroimaging for epilepsy have magnetic resonance imaging.	Audit	Consultant	TBC	Local clinical practice group
Children and young people with epilepsy are seen by an epilepsy specialist nurse who they can contact between scheduled reviews.	Audit	Specialist Nurse	TBC	Local clinical practice group

There is a national audit- Epilepsy 12 – conducted by RCPCH (Royal College of Paediatrics & Child Health) and data from the unit should be submitted as per requirement.

Supporting Documents and Key References

1. MHRA- new patient safety alert November 2023
2. NICE guideline (NG217)- Epilepsies in children, young people and adults. Published 27 April 2022 https://www.nice.org.uk/guidance/ng217

3. A practical clinical definition of epilepsy. Epilepsia, 55(4):475–482, 2014.

4. Management of Status Epilepticus- Children UHL guideline

5. Epilepsy and pregnancy- UHL guideline
6. RCPCH Document- Safety-netting information following a first seizure without a fever in children and young people.

Support group websites-

https://www.epilepsysociety.org.uk/
https://www.epilepsy.org.uk/
https://www.epilepsyresearch.org.uk/

Glossary

- Seizure - A seizure can be epileptic or non-epileptic. A paroxysmal abnormality of motor, sensory, autonomic or cognitive function.

- Epileptic seizure - Paroxysmal abnormality of motor, sensory, autonomic, cognitive function due to transient dysfunction of the cerebral cortex characterised by excessive and hypersynchronous neuronal activity.

- Non-epileptic seizure - Paroxysmal abnormality of motor, sensory, autonomic or cognitive function not due to an epileptic seizure.

- Febrile seizure - A seizure occurring in the presence of fever (> 37.8°C) or where history or clinical findings is suggestive of febrile seizures.

- Epilepsy - A group of chronic neurological conditions characterised by recurrent epileptic seizures.

- CAE - Childhood Absence Epilepsy

- JAE - Juvenile Absence Epilepsy

- JME - Juvenile Myoclonic Epilepsy

- CED – Children's Emergency Department

- EEG - Standard Electroencephalogram

- QTc - Corrected QT interval

- Self-limited epilepsy with centrotemporal spikes OR CECTS - Childhood Epilepsy with Centrotemporal Spikes (previously Benign Epilepsy with Centrotemporal Spikes/ Benign rolandic epilepsy)

- AED - Anti Epileptic Drug

Keywords

AED –Anti Epileptic Drug, Epilepsy, Epileptic, Seizure, Valproate

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details	
Guideline Lead (Name and Title) M. Joshi - Consultant	**Executive Lead** Chief Medical Officer
Details of Changes made during review: V 5- Sodium Valproate medication – national patient safety alert November 2023 reviewed and acted accordingly regarding sodium valproate medication. NICE guideline under review. Further update may be needed after reviewing in updated NICE guideline once available to comply with national recommendation for epilepsy management. V 4- Title of document changed from Recurrent afebrile seizure: newly diagnosed epilepsy to - Afebrile seizure: newly diagnosed epilepsy. Recent NICE guidance reviewed and updated local guideline accordingly with regards to medications. Glossary added.	