Epilepsy

An epilepsy is defined as a neurological condition characterised by recurrent epileptic seizures unprovoked by any immediately identifiable cause. An epileptic seizure is the clinical manifestation of an abnormal and excessive discharge of a set of neurons in the brain.

Epilepsy should be viewed as a symptom of an underlying neurological disorder and not as a single disease entity. The term ‘epilepsies’ is used in the title of the guideline to reflect this.

Diagnosis

Epilepsy is primarily a clinical diagnosis based on a detailed description of the events before, during and after a seizure given by the person and/or witness. The diagnosis of epilepsy requires that seizure type, epilepsy syndrome and any underlying cause are determined. It can be difficult to make a diagnosis of epilepsy and misdiagnosis is common.

The AED (anti-epileptic drug) treatment strategy should be individualised according to the seizure type, epilepsy syndrome, co-medication and co-morbidity, the child, young person's lifestyle, and the preferences of the person, their family and/or carers as appropriate.

Following a first seizure

- Children and young people presenting to an Accident and Emergency department following a suspected seizure should be screened initially, by a paediatric physician with onward referral to a specialist when an epileptic seizure is suspected or there is diagnostic doubt.
- A detailed history should be taken from the child, young person or adult and an eyewitness to the attack, where possible, to determine whether or not an epileptic seizure is likely to have occurred.
- The clinical decision as to whether an epileptic seizure has occurred should then be based on the combination of the description of the attack and different symptoms. Diagnosis should not be based on the presence or absence of single features.
- In a child or young person presenting with an attack, a physical examination should be carried out. This should address their cardiac, neurological and mental status, and should include a developmental assessment where appropriate.
- It may not be possible to make a definite diagnosis of epilepsy. If the diagnosis cannot be clearly established, further investigations (see later) should be considered. Follow-up should always be arranged.
- Where non-epileptic attack disorder is suspected, suitable referral should be made to psychological or psychiatric services for further investigation and treatment.
- Prospective recording of events, including video recording and written descriptions, can be very helpful in reaching a diagnosis.

Investigations

Information should be provided to children, young people and adults and families and/or carers as appropriate on the reasons for tests, their results and meaning, the requirements of specific investigations, and the logistics of obtaining them.

Electroencephalogram (EEG)

1. An EEG should be performed only to support a diagnosis of epilepsy in adults in whom the clinical history suggests that the seizure is likely to be epileptic in origin.

2. An EEG should be performed only to support a diagnosis of epilepsy in children and young people. If an EEG is considered necessary, it should be performed after the second epileptic seizure but may, in certain circumstances, as evaluated by the specialist, be considered after a first epileptic seizure.
3. An EEG should **not** be performed in the case of probable syncope because of the possibility of a false-positive result.
4. 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.
5. The EEG should not be used in isolation to make a diagnosis of epilepsy.
6. An EEG may be used to help determine seizure type and epilepsy syndrome in children and young people in whom epilepsy is suspected. This enables them to be given the correct prognosis.
7. In children and young people presenting with a first unprovoked seizure, unequivocal epileptiform activity shown on EEG can be used to assess the risk of seizure recurrence.
8. For children and young people in whom epilepsy is suspected, but who present diagnostic difficulties, specialist investigations should be available.
9. Repeated standard EEGs may be helpful when the diagnosis of the epilepsy or the syndrome is unclear. However, if the diagnosis has been established, repeat EEGs are not likely to be helpful.
10. Repeated standard EEGs should not be used in preference to sleep or sleep deprived EEGs.
11. When a standard EEG has not contributed to diagnosis or classification, a sleep EEG should be performed.
12. In children and young people, a sleep EEG is best achieved through sleep deprivation.

Neuroimaging

- Neuroimaging should be used to identify structural abnormalities that cause certain epilepsies.
- MRI should be the imaging investigation of choice in children and young people with epilepsy.
- MRI is particularly important in those:
    - who develop epilepsy before the age of 2 years or in adulthood
    - who have any suggestion of a focal onset on history, examination or EEG (unless clear evidence of benign focal epilepsy) in whom seizures continue in spite of first-line medication.
- Neuroimaging should ***not*** be routinely requested when a diagnosis of idiopathic generalised epilepsy has been made.
- CT should be used to identify underlying gross pathology if MRI is not available or is contraindicated.
- In an acute situation, CT may be used to determine whether a seizure has been caused by an acute neurological lesion or illness.

Other tests

- In children, appropriate blood tests (for example, plasma electrolytes, glucose, calcium) to identify potential causes and/or to identify any significant comorbidity should be considered.
- Other investigations, including blood and urine biochemistry, should be undertaken at the discretion of the specialist to exclude other diagnoses, and to determine an underlying cause of the epilepsy.
- In children and young people, a 12-lead ECG should be considered in cases of diagnostic uncertainty.
- In cases of diagnostic uncertainty, a referral to a cardiologist should be considered.

Classification

Epileptic seizures and epilepsy syndromes in children should be classified using a multi-axial diagnostic scheme. The axes that should be considered are: description of seizure (ictal phenomenology); seizure type; syndrome and aetiology.

The seizure type(s) and epilepsy syndrome, aetiology, and co-morbidity should be determined, because failure to classify the epilepsy syndrome correctly can lead to inappropriate treatment and persistence of seizures.

Management

Pharmacological treatment

The AED (anti-epileptic drug) treatment strategy should be individualised according to the seizure type, epilepsy syndrome, co-medication and co-morbidity, the child, young person's lifestyle, and the preferences of the person, their family and/or carers as appropriate.

Note: see table for further details of pharmacological treatment.

General information about pharmacological treatment

- Treatment with AED therapy is generally recommended after a second epileptic seizure.
- The diagnosis of epilepsy needs to be critically evaluated if events continue despite an optimal dose of a first-line AED.
- It is recommended that children and young people should be treated with a single AED (monotherapy) wherever possible. If the initial treatment is unsuccessful, then monotherapy using another drug can be tried. Caution is needed during the changeover period.
- If an AED has failed because of adverse effects or continued seizures, a second drug should be started (which may be an alternative first-line or second-line drug) and built up to an adequate or maximum tolerated dose and then the first drug should be tapered off slowly.
- If the second drug is unhelpful, either the first or second drug may be tapered, depending on relative efficacy, side effects and how well the drugs are tolerated before starting another drug.
- It is recommended that combination therapy (adjunctive or 'add-on' therapy) should only be considered when attempts at monotherapy with AEDs have not resulted in seizure freedom. If trials of combination therapy do not bring about worthwhile benefits, treatment should revert to the regimen (monotherapy or combination therapy) that has proved most acceptable to the child or young person, in terms of providing the best balance between effectiveness in reducing seizure frequency and tolerability of side effects.
- If using carbamazepine, offer controlled-release carbamazepine preparations.

Continuation of pharmacological treatment

Regular blood test monitoring in children and young people is not recommended as routine, and should be done only if clinically indicated and recommended by the specialist.

Indications for monitoring of AED blood levels are: detection of non-adherence to the prescribed medication

- suspected toxicity
- adjustment of phenytoin dose
- management of pharmacokinetic interactions (for example, changes in bioavailability, changes in elimination, and co-medication with interacting drugs)
- specific clinical conditions, for example, status epilepticus ad organ failure.

Withdrawal of pharmacological treatment

- The risks and benefits of continuing or withdrawing AED therapy should be discussed with children, young people and adults, and their families and/or carers as appropriate, who have been seizure free for at least 2 years.
- When AED treatment is being discontinued in a child, young person or adult who has been seizure free, it should be carried out slowly (at least 2–3 months) and one drug should be withdrawn at a time.
- Particular care should be taken when withdrawing benzodiazepines and barbiturates (may take up to 6 months or longer) because of the possibility of drug-related withdrawal symptoms and/or seizure recurrence.
- There should be a failsafe plan agreed with children, young people and adults and their families and/or carers as appropriate, whereby if seizures recur, the last dose reduction is reversed and medical advice is sought.

Table 1 AED options by seizure type

Seizure type	First-line AEDs	Adjunctive AEDs	Other AEDs that may be considered on referral to tertiary care	Do not offer AEDs (may worsen seizures)
Generalised tonic–clonic	Carbamazepine Lamotrigine Oxcarbazepinea Sodium Valproate	Clobazama Lamotrigine Levetiracetam Sodium valproate Topiramate		(If there are absence or myoclonic seizures, or if JME suspected) Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Tonic or atonic	Sodium Valproate	Lamotrigine	Rufinamide Topiramate	Carbamazepine Gabapentin Oxcarbazepine Pregabalin Tiagabine Vigabatrin
Absence	Lamotrigine Sodium Valproate	Lamotrigine Sodium Valproate	Clobazama Clonazepam Levetiracetam Topiramate Zonisamide	Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Myoclonic	Levetiracetam Sodium valproate Topiramate	Levetiracetam Sodium valproate Topiramatea	Clobazama Clonazepam Piracetam Zonisamidea	Carbamazepine Gabapentin Oxcarbazepine Phenytoin Pregabalin Tiagabine Vigabatrin
Focal	Carbamazepine	Carbamazepine	Lacosamide	

	Lamotrigine Levetiracetam Oxcarbazepine Sodium Valproate	Clobazama Gabapentin Lamotrigine Levetiracetam Oxcarbazepine Sodium valproate Topiramate	Phenobarbital Phenytoin Pregabalin Tiagabine Vigabatrin Zonisamide	
Infantile spasm	Steroid Vigabatrin			
Infantile spasm due to tuberous sclerosis	Vigabatrin			

Guidelines for Treating Convulsive Status Epilepticus in Children

Status epilepticus is a medical emergency that should be anticipated in any patient who presents with an acute seizure.

Definitions:

It is defined as continuous seizure activity or recurrent seizure activity without regaining of consciousness lasting for >30 min. Some have advocated 5 min (rather than 30) as the time limit, but others have suggested using the term impending status epilepticus for seizures between 5 and 30 min. The measures used to treat status epilepticus need to be started in any patient with acute seizures that do not stop within a few minutes.

The most common type is **convulsive status epilepticus** (generalized tonic, clonic, or tonic-clonic), but other types do occur, including **nonconvulsive status** (complex partial, absence), myoclonic status, epilepsia partialis continua, and neonatal status epilepticus.

Refractory status epilepticus is status epilepticus that has failed to respond to therapy, usually with at least 2 (although some have specified 3) medications.

Treatment Protocol for Status Epilepticus in Children

(Ref. NICE guidelines 2013)

Time 0 mins (1st step)	Seizure starts **Check ABC, O_2 inhalation** **Check Blood Glucose**	Confirm clinically that it is an epileptic seizure
5 mins (2nd step)	**Midazolam 0.1–0.2 mg/kg I.V bolus**	Midazolam may be given by parents Carers or ambulance crew in non-hospital setting
15 mins (3rd step)	**Midazolam 0.1–0.2 mg/kg I.V bolus**	This step should be in hospital **Consult Senior** **Prepare Phenytoin for 4th step** Re-confirm it is an epileptic seizure
25 mins (4th step)	**Phenytoin** 20 mg/kg by intravenous infusion over 20 mins or (if on regular phenytoin) **Phenobarbital 20 mg/kg IV** over 5 mins	Paraldehyde 0.8 ml/kg of mixture may be given after start of phenytoin infusion as directed by senior staff Inform intensive care unit and/or senior anesthetist
45 mins (5th step)	**Rapid Sequence Intubation** and anesthesia **Thiopental sodium 4 mg/kg IV**	Transfer to paediatric intensive care unit

When the protocol is initiated it is important to consider what pre-hospital treatment has been received and to modify the protocol accordingly.

Further management after cessation of seizure:

- Obtain further history*:* Recent trauma, infection, ingestion, drug history, seizure history
- Further investigations: (as indicated by clinical presentation and history if not done on initial presentation)
  Blood culture; blood gas; clotting studies, liver enzymes; lumbar puncture (should be deferred until cessation of clinical seizure); imaging (CT head)
- In selected patients:

– *Plasma*: ammonia, lactate, amino acids;
– *Urine*: organic acids, toxicology

Non-convulsive status epilepticus

Treatment for non-convulsive status epilepticus is less urgent than for convulsive status epilepticus. Treatment should be considered as follows:

- Maintenance or reinstatement of usual oral AED therapy
- Use of intravenous benzodiazepines under EEG control, particularly if the diagnosis is not established
- Referral for specialist advice and/or EEG monitoring.

Aftercare

- All children having had a prolonged seizure will need hospital admission for observation and if necessary further investigations. Admission to MICU is indicated if there are concerns about maintenance of airway, depressed neurological state, a need for continuing cardiac monitoring (Phenytoin) or when significant amounts of drugs have been required.
- Children reaching step 4 will need ITU.
- For **raised intracranial pressure**

– consider use of Mannitol 250-500mg/kg IV over 30-60mins;
– Maintain head up position 20º and head in line;
– Maintain PCO2 4.5-5.5 kPa.

- Consider Dexamethasone for oedema around a brain space occupying mass, 500microgms/kg bd.
- Catheterise as a full bladder can aggravate raised intracranial pressure.
- Treat pyrexia with PR or IV paracetamol.
- Give IV antibiotics if not already administered if serious infection cannot be excluded, LP is contraindicated and will need to be deferred.
- Ensure ongoing homeostasis , maintaining normoglycaemia, serum sodium between 135-145 mmol/l
- Insert NG tube and aspirate stomach contents if reduced level of consciousness or intubated.
- Support ventilation if hypoventilation is present.
- Review causes of status epilepticus and review current antiepileptic medication if appropriate.
- Review need for future rescue medication and care plan.