

# **EPILEPSY**

## **GUIDELINES AND PATHWAYS FOR CHILDREN AND YOUNG PEOPLE**



## Citation

This document and links to all other documents referred to in this document (patient information sheets etc.) are available at <https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>

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# Contributors

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The New Zealand paediatric neurologists are thanked for their contribution to the development of the Epilepsy Guideline and Pathway for Children and Young People.

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Epilepsy Technical Advisory Group – convened by the Ministry of Health  
Paediatric Neurology Clinical Network  
New Zealand League Against Epilepsy

It was supported by the Paediatric Society of New Zealand and Epilepsy New Zealand.

# Glossary

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ACC – Accident Compensation Corporation

ASM – Anti-seizure medication

BD – twice daily

BP – Blood Pressure

CGD – Carbohydrate-Deficient Glycoprotein syndromes

Cl – Chloride

CSF – Cerebrospinal Fluid

CT – Computed Tomography

DHB – District Health Board

DWI – Diffusion weighted imaging

ECG – Electrocardiogram

ED – Emergency Department

EEG – Electroencephalogram

FLAIR – Fluid-attenuated inversion recovery

GABA – GABA transaminase – an enzyme inhibitor

GLUT<sub>1</sub> – deficiency syndrome

GP – General Practitioner

GTCS – Generalised Tonic Clonic Seizure

HLA-B – Human Leukocyte Antigen – B

ILAE – International League Against Epilepsy

IR – Inversion Recovery

JME – Juvenile Myoclonic Epilepsy

K – Potassium

MRI – Magnetic Resonance Imaging

MTHFR – Methylene Tetrahydrofolate Reductase

Na – Sodium

NCL2 – Neuronal Ceroid Lipofuscinosis type 2

NEAD – Non-epileptic attack disorder

NICE – National Institute for Health Care and Excellence

NZLAE – New Zealand League Against Epilepsy

PET – Paediatric Epilepsy Training

QID – four times daily

REM – Rapid Eye Movement

RMO – Registered Medical Officer

SUDEP – Sudden Unexplained Death from Epilepsy

SWI – Susceptibility weighted imaging

TID – three times daily

# Introduction

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This guideline has been developed as part of a quality improvement project for childhood epilepsy. It is a collaborative effort from the Ministry of Health National Service Improvement Programme for Epilepsy, the Paediatric Society's Paediatric Neurology Clinical Network and the New Zealand League Against Epilepsy (NZLAE).

The guideline was adapted from the NICE paediatric epilepsy guidelines (NICE, 2016) and are evidence based where evidence exists. Its purpose is to define best practice for epilepsy care for New Zealand children.

We recognise that, due to limited resources at the present time, that some regions are unlikely to be able to provide the recommended standard of care in these guidelines.

We hope that by publishing and promoting a best practice guideline for epilepsy diagnosis and management of New Zealand children that all DHBs will move towards ensuring that a child's geographical location does not preclude them from receiving that standard of care.

This guideline recommends that children with epilepsy are diagnosed and managed by a paediatrician who:

- diagnoses and manages children with epilepsy as part of their general paediatric duties
- receives support and mentoring by a specified paediatric neurologist or group of paediatric neurologists
- participates in epilepsy professional development.

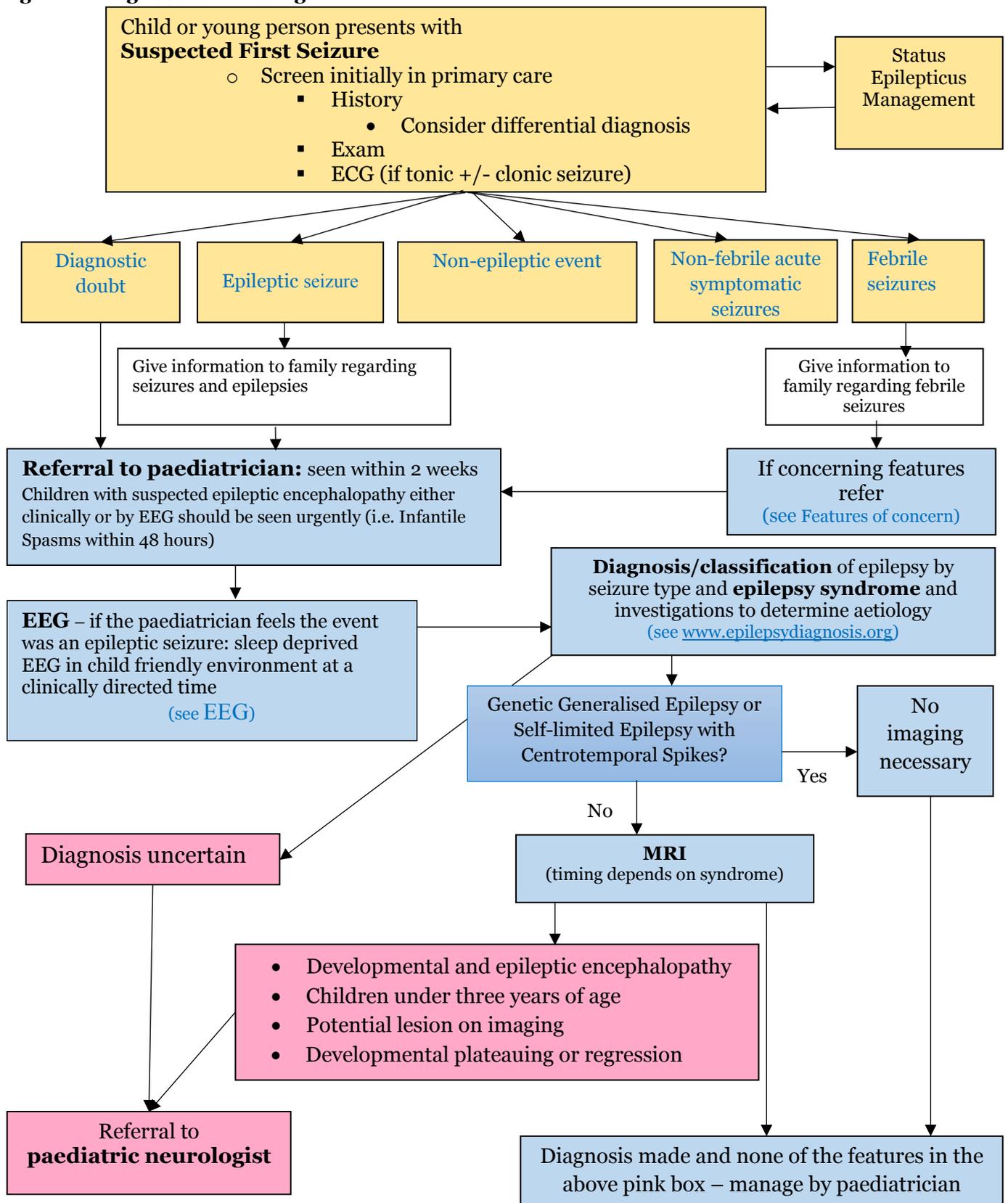
The recommended epilepsy professional development courses are the Paediatric Epilepsy Training (PET) courses. These courses were established and managed by the British Paediatric Neurology Association and are an internationally recognised accreditation for paediatricians who manage children with epilepsy. They will be regularly provided in New Zealand.

PET courses are designed specifically for paediatricians and and lectures and small group workshops with video based case studies. Ideally paediatricians who manage children with epilepsy will complete PET 1 (1 day), PET 2 (2 days) and PET 3 (2 days) or other equivalent training within a five year period as part of their continuing medical education. PET 1 is also appropriate for health professionals who see children with epilepsy in their practice including emergency department (ED) physicians, general practitioners, nurses and other allied health professionals.

This guideline is not meant to be a comprehensive epilepsy text but rather a recommended structure for diagnosis and management. The expectation is that the provider of care will have the appropriate experience, ongoing epilepsy training and support to supplement and or adapt the guidelines as appropriate. To keep these guidelines brief and readable specific evidence and referencing for each recommendation is not included. For more information regarding evidence please refer to the NICE epilepsy guidelines (<https://www.nice.org.uk/guidance/qs27>).

# Epilepsy diagnosis and management flow chart

Figure 1: Diagnosis and management



Note: Items in yellow boxes are generally initially performed by ED physicians, registered medical officers (RMOs) and general practitioners; items in blue boxes are generally performed by paediatricians; the pink boxes relate to paediatric neurology referral.

# Terminology and definitions

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The terminology and definitions used in this document are based on the International League Against Epilepsy (ILAE) position papers which can be found on the ILAE website at <https://www.ilae.org/guidelines/definition-and-classification>

- A practical clinical definition of epilepsy (Fisher, et al., 2014). *Epilepsia* 55 (4): 475 – 482
- Operational classification of seizures types by the ILAE: Position paper of the ILAE Commission for Classification and Terminology. (Fisher, et al., 2017). *Epilepsia* 58 (4) 522 - 530
- ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. (Sheffer, et al., 2017). *Epilepsia* 58 (4) 512 - 521

## Epileptic seizure

An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. A ‘non-epileptic seizure’ can look the same but is the consequence of a different ‘non-epileptic’ mechanism.

## Developmental and epileptic encephalopathy

The ILAE has introduced new terms which encompass epilepsy syndromes that have developmental slowing or regression associated with epilepsy. The first term, *Epileptic Encephalopathy*, is used when seizures and/or interictal electroencephalogram (EEG) abnormality impact negatively on development. The second term, *Developmental Encephalopathy*, reflects that abnormal development is related to the underlying pathophysiology, independent of seizures or EEG abnormality. When used together, the term *Developmental and Epileptic Encephalopathy* applies to the situation when the abnormal development is due to both the epilepsy and the underlying pathophysiology. If a child with a developmental encephalopathy has epileptic seizures which do not impact negatively on development, the term *Developmental Encephalopathy with Epilepsy* can be used.

## Genetic generalised epilepsy

Within the generalised epilepsies is a well-recognised and common subgroup of epilepsy syndromes which includes ‘childhood absence epilepsy’, ‘juvenile absence epilepsy’, ‘juvenile myoclonic epilepsy’ and ‘generalised tonic-clonic seizures alone’. These were previously known as the ‘idiopathic generalised epilepsies’. The concept of the genetic epilepsies is that they result from a known or presumed genetic mutation in which seizures are a core symptom. There is often no family history and often the underlying genes are not yet known. The genetic aetiology of these syndromes has been determined by twin and family studies.

# Seizures

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On initial presentation the child should be seen by medical staff with experience in managing children (GP, ED physician or paediatrician).

	<b>All children at presentation require:</b>
	<input type="checkbox"/> History
	<input type="checkbox"/> Exam
	<input type="checkbox"/> Acute investigations
	<input type="checkbox"/> Diagnosis

## History

1. Obtain and record detailed history of event from witness and child including the sequence of events, the presence or absence of focal features and the level of awareness throughout the seizure.
  - a. What were they doing at the time?
  - b. Circumstances of the event? (e.g. trigger)
  - c. Was there any aura?
  - d. Was there any impairment of awareness?
  - e. Was there any movement during the event?
  - f. Were there any focal features during the event?
  - g. Were there any symptoms after the event? (specifically ask about Todd's Paresis)
  - h. What was the duration of the event? (prolonged =>5 minutes)
2. Ask for and review any available video. Record description of video event.
3. Ask about previous seizures– it is important to ask about other previous possible events which the family may or may not have recognised as seizures.
  - a. Absence seizures
  - b. Myoclonic seizures
  - c. Focal aware seizures with aura only
  - d. Unwitnessed seizures in sleep – ask the following:
    - i. new onset nocturnal incontinence
    - ii. excessive salivation or blood on pillow
    - iii. unusual drowsiness or behaviour on morning waking.
4. Family history of young sudden death, epilepsy or arrhythmic disorders.
5. Developmental history and assessment.
6. Consider non-epileptic seizure differential diagnosis (see Differential for paroxysmal event). For more information on these seizure mimickers please refer to 'epilepsy imitators' at <https://www.epilepsydiagnosis.org/epilepsy-imitators.html> .

## Exam

7. Detailed physical examination including:
  - a. temperature
  - b. blood pressure
  - c. Woods' lamp examination in fair skinned children for neurocutaneous stigmata should be performed if equipment is available
  - d. neurological exam
  - e. cardiac exam
  - f. mental status examination.

## Acute investigations



All children with a tonic and/or clonic seizure require a 12-lead ECG

- Blood glucose and consider calcium measurement for tonic clonic seizures. Laboratory tests should not be routinely requested but rather ordered based on individual clinical circumstances as suggested by history.
- Neuroimaging is not usually required acutely.
  - Imaging, e.g. computed tomography (CT) brain, should be considered only when new focal deficits are noted on examination, the history or examination suggests head trauma, or following a first episode of status epilepticus.
- A 12 lead ECG for evidence of long QT syndrome for tonic and/or clonic seizures.
- Consider toxic drug and alcohol screen if drug ingestion possible or the patient is an adolescent.
- EEG.
  - It is recognised that physicians who do not regularly manage children with epilepsy consequently have less experience in differentiating epileptic seizures from non-epileptic seizures. They are more likely to order unnecessary EEGs in children and interpret normal or abnormal results incorrectly.
  - It is generally not necessary to request an EEG from the ED department for a single seizure.
  - If the child has had more than one epileptic seizure, or a prolonged epileptic seizure, an ED physician or unsupervised paediatric RMO should request an EEG **after discussion** with a paediatrician or paediatric neurologist. If after discussion with the paediatrician or paediatric neurologist an EEG is ordered from ED the report should be sent to the paediatrician who was consulted and that paediatrician should arrange to follow up the child.

## Diagnosis of one of the following should be made:

- ✚ Febrile seizure – see [Febrile seizures](#)
- ✚ Acute symptomatic seizure – see [Non-febrile acute symptomatic seizures](#)
- ✚ Single epileptic seizure
- ✚ Epilepsy - see [Classification of epilepsy by seizure type, epilepsy type and epilepsy syndrome](#)
- ✚ Non Epileptic Event – see [Differential for paroxysmal event](#)

## Management of epileptic seizures

1. Preventative treatment with anti-seizure medications (ASMs) is not initiated at this stage.
  - a. An exception may rarely occur if the child is admitted with multiple epileptic seizures or status in which case the decision to treat should be discussed with the paediatrician or paediatric neurologist.
2. Provision of prescription of rescue/emergency medication should be given to families of children over three months with prolonged febrile or afebrile tonic and/or clonic seizures (i.e. five minutes or longer). Buccal midazolam is the preferred medication and route.
  - a. Buccal midazolam (for intranasal administration use local protocol with an atomiser):
    - i. 3 – 11 months: 2.5mg
    - ii. 1 – 4 years: 5mg
    - iii. 5 - 9 years: 7.5mg
    - iv. 10 - 18 years: 10mg

Prescribe plastic ampoules 15mg/3ml

- b. Rectal diazepam:
      - i. 0.3-0.5mg/kg/dose (max dose usually 10mg).
      - ii. Dose may only be repeated under medical supervision
      - iii. Delayed respiratory depression may occur after rectal administration.
2. Education should be provided to child and family/care giver on the following topics: Patient information documents for each of the topics below are found on the Paediatric Neurology Clinical Network <https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>. Alternatively, families should be referred to the seizure and epilepsy information on the Kidshealth website where there are videos and PDFs they can download. <https://www.kidshealth.org.nz/what-if-my-child-has-had-epileptic-seizure> and <https://www.kidshealth.org.nz/epilepsy-children>
  - a. Explanation about what epileptic seizures are and what the preliminary diagnosis of the child is. (e.g. febrile seizure, single epileptic seizure, epilepsy)
  - b. Explanation of risk of recurrence for diagnosis.

- c. First aid epileptic seizure management:
    - i. The child should be laid on the floor away from objects that may cause harm
    - ii. Attempts to open the child's mouth should not be made
    - iii. Phone for ambulance if seizure lasts longer than five minutes
    - iv. Place in the left lateral (recovery) position during post ictal period
  - d. Reasonable precautions to be discussed with caregivers include:
    - i. Direct supervision by an adult when the child has access to water (this includes bathing)
    - ii. Avoid bike riding in any traffic
    - iii. Avoid climbing to heights greater than one metre (exception is a playground with safety mats)
  - e. Usually long term treatment with an ASM is not indicated after the first afebrile epileptic seizure or febrile seizures.
  - f. Use of rescue medication if indicated – provide prescription and information sheet: <https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>
  - g. Recommend the family record any future events on video if possible.
3. Best practice recommends the child should be seen by a **paediatrician** either during acute assessment or as outpatient follow-up within two weeks of presentation for afebrile seizures. No follow up is necessary for febrile seizures unless they have features of concern (see Features of concern).
4. Child should be admitted to the ward:
- a. if they have had recurrent seizures within a 24 hour period
  - b. if they are not recovering after the seizure
  - c. if they have a focal deficit
  - d. if they are encephalopathic
  - e. if treating physician feels admission would be advantageous.

# Seizures with fever

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An epileptic seizure that presents in the context of a fever can be either:

1. An acute symptomatic epileptic seizure (e.g. in a child with meningitis or encephalitis)
2. A febrile seizure
3. An epileptic seizure in an individual with epilepsy in whom the seizure is triggered by a fever or illness

## Lumbar puncture

Lumbar puncture should be performed in all children less than six months of age who have a fever and an epileptic seizure unless contraindicated.

## Febrile seizures

Febrile Seizure is a diagnosis given to children who have epileptic seizures only with fever between the age of six months and six years. This has previously been referred to as Febrile Convulsions. A child presenting with a febrile epileptic seizure has the same risk for serious sepsis as another child of the same age presenting with fever alone. A child who has had a febrile seizure should be investigated and managed according to the same criteria used for other children presenting with a febrile illness.

## Features of concern

Children with a diagnosis of febrile seizure do not require follow up unless they have **features of concern** which include any of the following:

- >3 seizures
- are under six months or over six years of age
- seizures longer than 30 minutes
- seizures that have focal signs
- seizures that are not generalised onset tonic clonic

Best practice recommends that a child with any of the above should see a paediatrician within two weeks.

Seizures occurring within the context of a gastrointestinal illness (regardless of temperature during the seizure) should be conceptualised and managed in the same way as febrile seizures.

# Non-febrile acute symptomatic seizures

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Epileptic seizures can be due to many non-epilepsy causes. The following need to be considered.

1. Metabolic causes (e.g. hypoglycaemia, hyponatraemia, hypernatraemia, hypocalcaemia)
2. Drugs - take history of illicit and prescribed drugs.
3. Anoxic seizure including breath holding attacks and faints
4. Acute cerebral pathology (see recommendations for [Neuroimaging](#))

# Classification of epilepsy by seizure type, epilepsy type and epilepsy syndrome

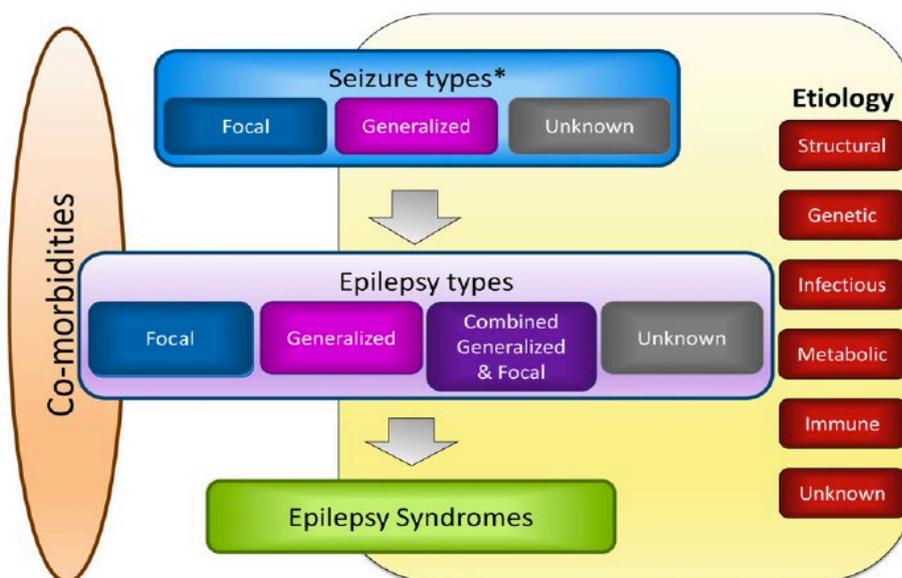
See - [www.epilepsydiagnosis.org](http://www.epilepsydiagnosis.org)

It is essential to determine the seizure type(s), epilepsy type, epilepsy syndrome, aetiology, and comorbidity, because failure to classify the epilepsy correctly can lead to inappropriate treatment and persistence of seizures.

Classify epileptic seizures, epilepsy type and epilepsy syndromes using a multi-axial diagnostic scheme. Consider the following axes: description of epileptic seizure (ictal phenomenology); seizure type; epilepsy type; epilepsy syndrome; aetiology and co-morbidities.

Give children and young people information about their seizure type(s), epilepsy type and epilepsy syndrome, and the likely prognosis (<https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network/>)

**Figure 2: Classification of the epilepsies**



\*Denotes onset of seizure. (Sheffer, et al., 2017), Epilepsia © ILAE

# Determining aetiology of epilepsy

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## EEG

An EEG does not rule in or rule out a diagnosis of epilepsy and should not be ordered if the clinician is unsure as to whether the events in question are epileptic seizures or not.

An EEG should be performed for all children who have epileptic seizures as it is essential for diagnosing epilepsy type and making an epilepsy syndrome diagnosis which in turn:

- directs therapy
- directs further investigations
- enables appropriate prognostic information to be given to the families.

EEGs should not be ordered for febrile seizures, acute symptomatic seizures or for events when the paediatrician is not sure if they are epileptic seizures.



### **Recommendation:**

An EEG should only be ordered after a child has been reviewed by a **paediatrician** who is sure the event is an epileptic seizure.

## First seizure

- It is recognised that physicians who do not regularly manage children with epilepsy have less experience in differentiating epileptic seizures from non-epileptic events and are more likely to order unnecessary EEGs in children. It is therefore recommended that an ED physician or unsupervised RMOs should not order an EEG after a first seizure.
- An EEG should be ordered by a paediatrician or paediatric neurologist and this should ideally be after they have assessed the child. If, after taking the history, they determine that the event was an epileptic seizure they will generally order an EEG after the first epileptic seizure.

## Second seizure

- EEG may be ordered by an ED physician or unsupervised RMO **after discussion** with the paediatrician when the child has had two or more epileptic seizures or a prolonged seizure at acute presentation. If this is the case and the physician requests an EEG from ED, the report should be sent to the paediatrician who was consulted and the paediatrician will arrange for follow up of the child. GPs should not order EEGs.

## Best practice recommendations for timing of the EEG

- Single epileptic seizure – within eight weeks (this should be expedited to within two weeks of presentation if the child has a subsequent epileptic seizure while waiting for an EEG).
- Two or more epileptic seizures – within two weeks
- Suspected developmental and epileptic encephalopathy – as soon as possible (e.g. within 48 hours for Infantile Spasms).

The EEG result helps determine the epilepsy syndrome which guides appropriate ASM choice. Best practice requires an EEG to be performed **prior to initiation of therapy**, however children should not be denied treatment due to a wait for EEG. Therefore, there will be instances when an EEG should be requested to be performed within a few days so therapy can be initiated.

All children should be sleep-deprived for their EEG.

EEGs should be reported by a paediatric neurologist (or a neurologist with training and experience in reading paediatric EEGs).

If Infantile Spasms are suspected clinically, the child should be referred urgently to a paediatric neurologist and an EEG should be requested urgently. Best practice recommends this be performed within 48 hours of the request (or 72 hours if a weekend).

## Neuroimaging

Use neuroimaging to identify structural abnormalities that cause certain epilepsies.

Do not routinely request neuroimaging when a diagnosis of Genetic Generalised Epilepsy (GGE) – i.e. Childhood Absence Epilepsy, Juvenile Absence Epilepsy, Juvenile Myoclonic Epilepsy, or Self-limited Epilepsy with Centrotemporal Spikes (CETS), previously called Benign Epilepsy with Centrotemporal Spikes (BECTS) has been made. If atypical features are present or the child does not respond to appropriate therapy, neuroimaging should be considered.

## Magnetic resonance imaging (MRI)

MRI is 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 three years
- who have any suggestion of a focal epileptic seizure onset on history, examination or EEG
- in whom epileptic seizures continue in spite of first-line medication.

For children who require an MRI, best practice recommendation for timing is as follows:

- Infantile Spasms: within 72 hours from the diagnosis as the result guides therapy
- developmental and epileptic encephalopathy: within two weeks
- focal epilepsy or generalised epilepsy that is not consistent with a genetic generalised epilepsy - within two months if no previous imaging. If previous imaging performed within 4 months.

The recommended MRI epilepsy protocol for children with seizures should be requested and followed.

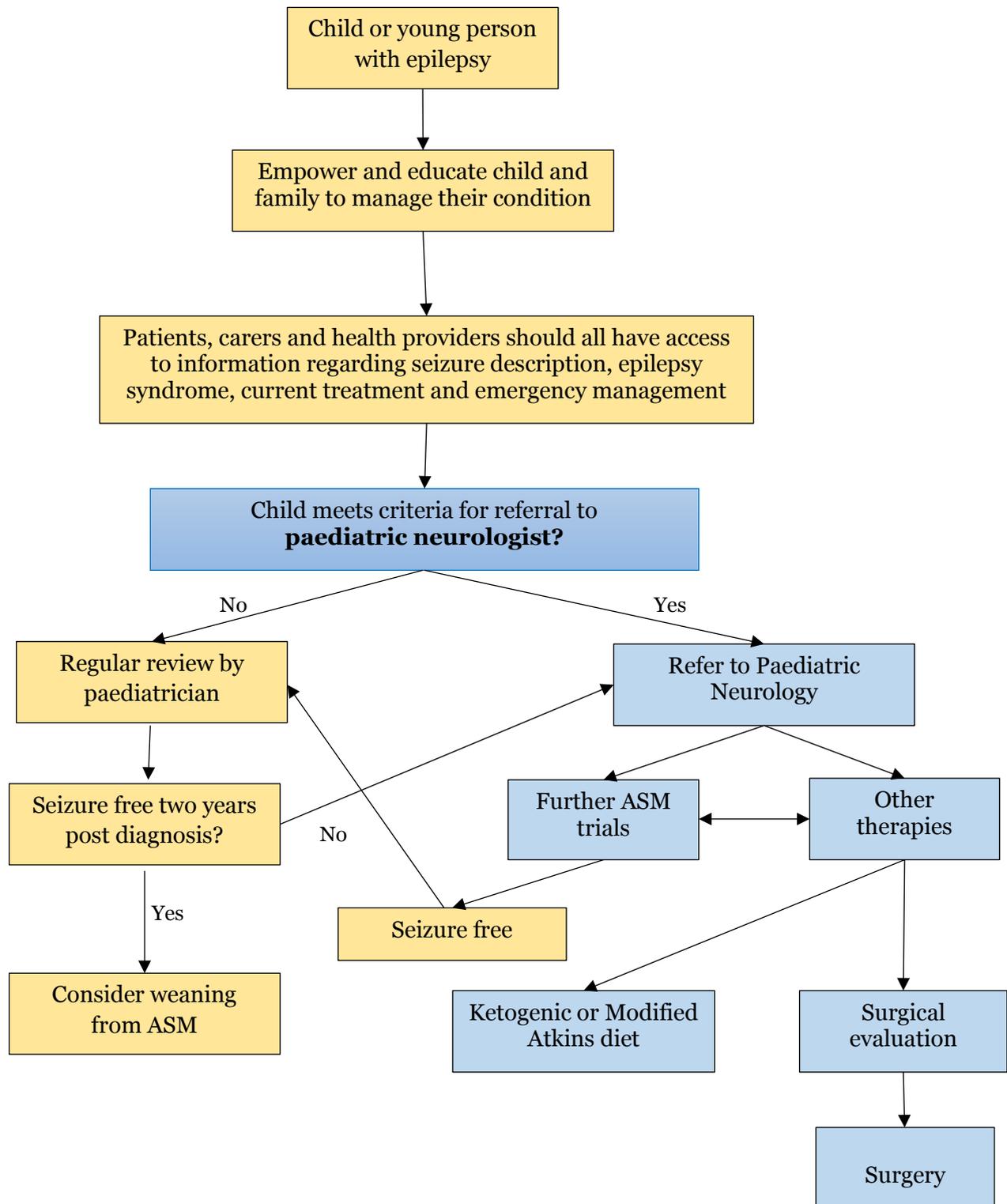
- 3D T1 whole brain with 1 mm 3 plane reconstruction of the whole brain
- Axial T2 FLAIR, DWI, SWI or T2 Star
- Coronal 2mm (2-3mm) FLAIR whole brain
- Sagittal 2mm (2-3mm) T2 whole brain
- If temporal lobe epilepsy is suspected, then add coronal inversion recovery (IR) and T2 cuts angled for temporal lobe.

## **Blood tests and other investigations**

Other investigations, including blood, cerebrospinal fluid (CSF) and urine samples should be undertaken at the discretion of the paediatrician or paediatric neurologist to exclude other diagnoses and to determine an underlying cause of the epilepsy.

# Managing epilepsy in children and young people

Figure 3: Managing epilepsy



# Overall care

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Provide a point of contact for the patient and family with specialist services. Depending on resources this may be the family GP or district health board (DHB) specialty nurse.

Adopt a consulting style that enables the child with epilepsy and their family and/or carers as appropriate, to participate as partners in all decisions about their healthcare, and take fully into account their race, culture and any specific needs.

Establish a comprehensive care plan that is agreed between the person, family and/or carers when appropriate, and primary care and secondary care providers. Include lifestyle issues as well as medical issues.

Epilepsy specialist nurses should be established and be integral to the network. Epilepsy specialist nurses where available, should be an integral part of the network of care of children and young people with epilepsy. Their key roles are to support both **paediatric neurologist** and **paediatrician**, to ensure access to community and multi-agency services and to provide information, training and support to the child, families, carers and, in the case of children, others involved in the child's education, welfare and wellbeing.

Epilepsy New Zealand (Epilepsy NZ) epilepsy educators, where available, should also be a part of the care team. They can provide valuable education to teachers, whānau and other individuals involved in the child's life. Where epilepsy specialist nurses are not available the Epilepsy NZ educators are able to fulfil some of the functions of epilepsy specialist nurses.

## Providing a regular structured review

Children and young people should have a regular structured review with a paediatrician or paediatric neurologist. It is important to remember seizure freedom is the aim. Infrequent tonic and/or clonic seizures are associated with an increased risk of sudden unexpected death from epilepsy (SUDEP). If seizure freedom cannot be achieved within two years or after two ASMs then the child should be referred to a paediatric neurologist.

### Frequency of the review

For children and young people, the maximum interval between reviews should be one year, but the frequency of reviews should be determined by the child's epilepsy and their wishes and those of the family and/or carers. The interval between reviews should be agreed between the child, their family and/or carers as appropriate, and the specialist, but is likely to be between three and 12 months.

#### **Recommendation**



If seizure free for six months review 12 monthly.

If not seizure free for six months then review should occur at least every three to six months.

## **At the review**

At the annual review, enquire about medication side effects and discuss the treatment plan to ensure concordance and adherence to medication.

At the review, ensure children have access to written and visual information, counselling services, information about community support organisations (e.g. Epilepsy NZ), epilepsy specialist nurses (if available), timely and appropriate investigations, and referral to tertiary services.

# Referral to tertiary care

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All children and young people with epilepsy should have access, via their specialist, to a paediatric neurologist when circumstances require.

## Information about tertiary epilepsy services

The tertiary service should include a multidisciplinary team, experienced in the assessment of children and young people with complicated epilepsy.

The expertise of multidisciplinary teams involved in managing complex epilepsy should ideally include psychology, social work, neuroradiology, clinical nurse specialists, neurophysiology, paediatric neurologist and dieticians. Teams should have MRI and video-EEG facilities available to them.

## When to refer to a tertiary epilepsy service

We aim to provide a service for children and young people with epilepsy which is equivalent with the United Kingdom NICE Guidelines for Epilepsy in Children (NICE, 2016).

All of the following children should therefore be referred for an assessment by a paediatric neurologist:

- Children and young people who are not seizure free within two years of diagnosis
- Children and young people who are not seizure free after a trial of two ASMs
- Children with seizure onset under three years of age
- Children and young people with potential neoplastic lesions on imaging (oncology service should also be consulted)
- Children with developmental plateauing or regression and seizures
- Children with suspected developmental and epileptic encephalopathy (including, but not limited to, Infantile Spasms, Dravet Syndrome, Epilepsy with Myoclonic Atonic Seizures, Lennox-Gastaut Syndrome, etc.)
- Children with EEG abnormalities that are not in keeping with the clinical presentation or are consistent with an encephalopathy
- Children with recognised conditions that place them at high risk of medically refractory epilepsy (e.g. tuberous sclerosis, Sturge Weber).

## **Diagnostic doubt**

For children and young people in whom there is diagnostic doubt as to the nature of the events there should be a low threshold for referral to paediatric neurologist.

For children and young people in whom the paediatrician is unable to make a specific epilepsy syndrome diagnosis it is reasonable to refer for a paediatric neurological opinion.

The paediatric neurologist service will endeavour to see children with new onset developmental and epileptic encephalopathies as soon as possible. These should be referred and discussed with a neurologist urgently.

# Education and Information for Children and young persons with epilepsy

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Children and their families should be provided with oral and written epilepsy information. The information should contain essential up-to-date details about a child or young person's epilepsy, including their emergency care plan, current medication and key professional contacts. The purpose is to help children and young people with epilepsy and their families to communicate with healthcare and other professionals and to help healthcare professionals communicate with each other. It should be discussed and agreed between the child or young person with epilepsy, their parents and/or carers and their primary and secondary health and social care professionals. This information should be reviewed at least annually.

It is important to provide education and information to the child and family relating to the following questions and topics:

- What are seizures?
- What is epilepsy?
- What type of seizures does the child have?
- What type of epilepsy and specific epilepsy syndrome does the child's or young person have?
- What investigations may be needed?
- What happens in an EEG?
- What happens in an MRI?
- What treatment options are there?
- How effective are the treatments and what potential side effects are there?
- What things might trigger a seizure?
- What is the prognosis of the child's epilepsy?
- Why does the child have epilepsy?
- What is status epilepticus?
- What should the parents do if the child has a seizure? Information on rescue therapy if appropriate.
- When should the family call an ambulance or contact their family doctor?
- What precautions does the child and family need to take now that their child has had a seizure? Recommendations regarding swimming and bike riding. Driving laws.
- What is Sudden Unexplained Death in Epilepsy?
- What benefits and social services are available?
- Who should they tell about their child having epilepsy?
- Will the child's lifestyle, leisure and social activity be affected by their seizures and epilepsy?
- What organisations are available to provide additional information and support? Epilepsy New Zealand
- How do seizures, epilepsy and medications impact on contraception, family planning and pregnancy? It is important that all girls and their family (regardless of age) are informed about these issues.

Families can be referred to the seizure and epilepsy sections on the Kidshealth website where they can find videos and webpages with information that can be downloaded as a PDF:

<https://www.kidshealth.org.nz/tags/epilepsy> or <https://www.kidshealth.org.nz/what-if-my-child-has-had-epileptic-seizure> . Alternatively, information sheets for families covering these topics can be found on the Paediatric Clinical Networks Website in the Paediatric Neurology Clinical Network section at the following link.

<https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>

# Treating epilepsy with ASMs

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## Starting treatment with ASMs



ASM therapy in children and young people should be initiated by a paediatrician or paediatric neurologist.

The decision to initiate ASM therapy should be taken between the child and their family and/or carers (as appropriate) and the specialist (paediatrician or paediatric neurologist) after a full discussion of the risks and benefits of treatment. This discussion should take into account details of the person's epilepsy syndrome, comorbidities, prognosis and lifestyle. For all girls information regarding the effect of ASMs on the fetus should be given (see [Pregnancy](#)).

Provide information about ASMs for example indications, side effects and licence status.



Care givers should be given information regarding specific potential ASM side effects and told what to look for.

See New Zealand Formulary Information Leaflets for Parents and Carers – <https://www.nzfchildren.org.nz>

Some children (through their families and/or carers, in some instances) may choose not to take ASM therapy following a full discussion of the risks and benefits.

Treatment with ASM therapy is generally recommended after a second epileptic seizure. This includes individuals with a single seizure and a subsequent EEG in which other unrecognised seizures are identified.

### Starting ASMs after a 'first unprovoked epileptic seizure'

Consider ASM therapy and discuss with the child and their family and/or carers as appropriate after a first unprovoked seizure if seizure was prolonged or status epilepticus.

### Factors to consider when choosing which ASM to offer

Individualise the anti seizure medication (ASM) treatment strategy according to the **seizure type**, epilepsy type, **epilepsy syndrome**, co-medication and co-morbidity, the child's lifestyle, and the preferences of the child and their family and/or carers as appropriate. The availability of a suitable formulation for the child should also be considered. For girls, ASM effects on future pregnancies should be considered when choosing an ASM.

When possible, choose which ASM to offer on the basis of the presenting **epilepsy syndrome**. If the epilepsy syndrome is not clear at presentation, base the decision on the presenting **seizure type(s)** or **epilepsy type**.

## **How to use ASMs when treating epilepsy**

Treat with a single ASM (monotherapy) wherever possible.

If an ASM has failed because of adverse effects or continued seizures, start a second drug (which may be an alternative first-line or second-line drug) and build up to an adequate or maximum tolerated dose and then taper off the first drug slowly.

If the second drug is unhelpful, taper either the first or second drug, depending on relative efficacy, side effects and how well the drugs are tolerated before starting another drug.

Combination therapy may be more effective than monotherapy.

For special considerations in females of childbearing potential, and children under 3 years, see specific sections below.

## **How to continue ASM therapy and actions to take**

Continuing ASM therapy should be managed by the paediatrician. It should be part of the child's agreed treatment plan, which should include details of the specific drug, drug dosage, possible side effects, and action to take if seizures persist.

If management is straightforward, continuing ASM therapy can be prescribed by the child's GP if local circumstances and/or licensing allow but supervision by paediatrician continues.

The prescriber must ensure that the child and their family and/or carers as appropriate are fully informed about treatment including action to be taken after a missed dose or after a gastrointestinal upset.

Maintain a high level of vigilance for treatment-emergent adverse effects (for example, bone health issues and neuropsychiatric issues).

## **Treatment adherence**

Optimise adherence to treatment by:

- educating children and their families and/or carers in the understanding of their condition and the rationale of treatment
- using simple medication regimens
- adjusting ASMs to avoid or reduce adverse effects.
- advocate the use of weekly medicine organisers and daily medication alarms on smart phones

## Blood tests and monitoring ASM blood levels

Do not routinely carry out regular blood tests for either potential ASM side effects or ASM monitoring (exception phenytoin) – only do blood tests if clinically indicated.

If a child presents with any potential ASM side effects to their GP or paediatrician the threshold for blood tests should be low.

Indications for monitoring of ASM blood levels are:

- suspicion 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, organ failure and certain situations in pregnancy.

Examples of blood tests include:

- before surgery – platelets in those on sodium valproate

## Action to take if seizures persist on optimal ASM therapy

Compliance should be assessed. If compliance is adequate the diagnosis of epilepsy needs to be critically evaluated if events continue despite an optimal dose of a first-line ASM.

## Action to take in the event of seizure freedom

Discuss the risks and benefits of continuing or withdrawing ASM therapy with children and young people, and their families and/or carers after seizure freedom of two years.

The decision to continue or withdraw medication should be taken by the child or young person and their families and/or carers as appropriate, and the **specialist** (paediatrician or paediatric neurologist) after a full discussion of the risks and benefits of withdrawal. At the end of the discussion the risk of seizure recurrence on and off treatment should be understood. This discussion should take into account details of the child's epilepsy syndrome, prognosis and lifestyle.



Withdrawal of ASMs **must** be managed by, or be under the guidance of, the **paediatrician or paediatric neurologist**.

## **Stopping an ASM**

When ASM treatment is being discontinued in a child who has been seizure free, wean the ASM slowly (over at least two to three months) and withdraw one drug at a time.

Take particular care when withdrawing benzodiazepines and barbiturates (may take up to six months or longer) because of the possibility of drug-related withdrawal symptoms and/or seizure recurrence.

Agree a plan with children and their families and/or carers as appropriate, whereby if seizures recur, the last dose reduction is reversed and medical advice is sought.

# ASMs based on epilepsy syndrome

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Written information should be provided to the family for each ASM considered. Each ASM specified in this document (carbamazepine, sodium valproate, lamotrigine, ethosuximide, clobazam, levetiracetam, prednisone, topiramate, vigabatrin) has an information sheet for families available at the following link.

✚ New Zealand Formulary Information Leaflets for Parents and Carers:

<https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>

## Generalised Genetic Epilepsy

### Childhood Absence Epilepsy

- First-line treatment – ethosuximide
- Second-line treatment – sodium valproate or lamotrigine. If absence seizures persist at puberty, then it is important to reconsider ASM choice taking into account possible effects on pregnancy (see warning regarding fetal effects)



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

### Juvenile Absence Epilepsy

- First-line treatment – sodium valproate (consider lamotrigine or levetiracetam for girls of child bearing age)
- Second-line treatment – lamotrigine, levetiracetam, topiramate.

Negative effects on the fetus (teratogenic and developmental) need to be discussed with girls and their families considering using valproate. It is essential that appropriate contraception advice is given to all girls that might become sexually active.



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

## Juvenile Myoclonic Epilepsy (JME)

Offer sodium valproate as first-line treatment to children with newly diagnosed JME, unless it is unsuitable. Girls of childbearing age should consider trials of lamotrigine and levetiracetam first line prior to sodium valproate.

Negative effects on the fetus (teratogenic and developmental) need to be discussed with girls and their families considering using valproate. It is essential that appropriate contraception advice is given to all girls that might become sexually active.

Consider lamotrigine, levetiracetam or topiramate if sodium valproate is unsuitable or not tolerated. Be aware that topiramate has a less favourable side-effect profile than lamotrigine, levetiracetam and sodium valproate. Lamotrigine may exacerbate myoclonic seizures.



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

## Other genetic generalised epilepsies

Offer lamotrigine or sodium valproate as first-line treatment to children, with Epilepsy with Generalised Tonic-clonic (GTC) Seizures Only. Girls of childbearing age should consider trials of lamotrigine and levetiracetam first line prior to sodium valproate .

Negative effects on the fetus (teratogenic and developmental) needs to be discussed with girls and their families considering using valproate. It is essential that appropriate contraception advice is given to all girls that might become sexually active.

Consider topiramate and levetiracetam as second-line treatment.



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

## Focal Epilepsies

### Childhood Epilepsy with Centrotemporal Spikes and Panayiotopoulos Syndrome

Discuss with the child and their family and/or carers, whether ASM treatment for Self-limited Epilepsy with Centrotemporal Spikes or Panayiotopoulos Syndrome is indicated.

If therapy is required offer lamotrigine or carbamazepine as first-line treatment to children with Self-limited Epilepsy with Centrotemporal Spikes or Panayiotopoulos syndrome.

Consider levetiracetam as first line treatment if lamotrigine or carbamazepine are contraindicated.

Be aware that carbamazepine and oxcarbazepine may exacerbate or unmask continuous spike and wave during slow sleep, which may occur in some children with Childhood Epilepsy with Centrotemporal Spikes. Clinically this may present with learning and/or behavioural difficulties or more seizures.

Negative effects on the fetus needs to be discussed with girls and their families considering using ASMs. Avoid sodium valproate in focal epilepsies if possible in females. It is essential that appropriate contraception advice is given to all girls that might become sexually active.



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

Consider adjunctive treatment if a second well-tolerated ASM is ineffective.



#### **Note**

Children of South East Asian origin should be screened for HLA-B\*1502 haplotype via the Blood Bank prior to the initiation of carbamazepine - positive children should not receive carbamazepine.

## **Developmental and Epileptic Encephalopathies**

### **Dravet Syndrome**

At diagnosis of, or suspected diagnosis of Dravet Syndrome, discuss management with a paediatric neurologist. Best practice recommends the child should be referred to paediatric neurologist and seen within four weeks.

Consider sodium valproate or clobazam as first-line treatment in children with Dravet syndrome. Avoid lamotrigine and carbamazepine.

### **Infantile Spasms**

At diagnosis of, or suspected diagnosis of Infantile Spasms, management should be discussed urgently with a paediatric neurologist and best practice recommends the child be seen by the paediatric neurologist within four weeks.

Offer a steroid (prednisolone or tetracosactide) as first-line treatment to infants with Infantile Spasms that are not due to tuberous sclerosis.

- Prednisolone 10mg QID for two weeks
- If spasms persist after one week increase prednisolone to 20mg TID for remaining doses

- Taper prednisolone after two weeks at five day intervals
  - 10mg QID – 30mg per day/20mg per day/10mg per day/stop
  - 20mg TID - 40mg per day/20mg per day/10mg per day/stop
- Use omeprazole for ulcer prevention and consider oral antifungal for candida prevention
- Give instructions as to infectious contacts (particularly varicella) and vaccine precautions.
- Monitor blood pressure (BP) twice a week.
- If steroids are ineffective offer a trial of vigabatrin

Offer vigabatrin as first-line treatment to infants with Infantile Spasms due to tuberous sclerosis.

- BD dosing
- 50mg/kg/day for day one and two
- 100mg/kg/day for day three
- Increase to at least 150mg/kg/day if spasms continue after one week (maximum of 180mg/kg/day)
- Continue for three months
- Parents should be made aware of visual field side effects and the requirement for monitoring of this if remaining on vigabatrin for longer than six months.
- If vigabatrin is ineffective, offer a steroid (prednisolone or tetracosactide).

# ASMs based on seizure types and epilepsy types

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Written information should be provided to the family for each ASM considered. Each ASM specified in this document (carbamazepine, sodium valproate, lamotrigine, ethosuximide, clobazam, levetiracetam, prednisone, topiramate, vigabatrin) has an information sheet for families available at the following link.

- ✚ New Zealand Formulary Information Leaflets for Parents and Carers:  
<https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>

## Generalised epilepsy

### Absence seizures



#### Note

All epileptic seizures where children stare are not absence seizures – they may be focal impaired awareness seizures with altered awareness and no other features.

Offer ethosuximide as first-line treatment to children with absence seizures. If there is a high risk of GTC seizures, offer sodium valproate, unless it is unsuitable (e.g. girls of childbearing age with risk of pregnancy). Girls and their families need to be aware of teratogenic and developmental risks of sodium valproate. It is essential that appropriate contraception advice is given to all girls that might become sexually active.

Offer lamotrigine or leviteracetam if ethosuximide and sodium valproate are unsuitable, ineffective or not tolerated.



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

## Generalised tonic-clonic seizures

Offer sodium valproate as first-line treatment to children with newly diagnosed GTC seizures unless unsuitable (e.g. girls of childbearing age with risk of pregnancy). Girls and their families need to be aware of teratogenic and developmental risks of sodium valproate. It is essential that appropriate contraception advice is given to all girls those that might become sexually active.

In a child <3 years old the first-line is clobazam, levetiracetam, or lamotrigine. Avoid sodium valproate in children under three years if aetiology of epilepsy is unclear.



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

## Myoclonic seizures

Offer sodium valproate or clobazam as first-line treatment to children with newly diagnosed myoclonic seizures, unless it is unsuitable (e.g. girls of childbearing age with risk of pregnancy). Girls and their families need to be aware of teratogenic and developmental risks of sodium valproate. It is essential that appropriate contraception advice is given to all girls those that might become sexually active.

Consider levetiracetam or topiramate if sodium valproate is unsuitable (i.e. girls of childbearing age with risk of pregnancy) or not tolerated. Be aware that topiramate has a less favourable side-effect profile than levetiracetam and sodium valproate. Avoid sodium valproate in children under 3 years if aetiology of epilepsy is unclear.



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

## Tonic or atonic seizures

Offer clobazam or sodium valproate (unless it is unsuitable eg girls of childbearing age with risk of pregnancy) as first-line treatment. Girls and their families need to be aware of teratogenic and developmental risks of sodium valproate. It is essential that appropriate contraception advice is given to all girls those that might become sexually active. Avoid sodium valproate in children under 3 years if aetiology of epilepsy is unclear.



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

## Focal epilepsy and focal seizures

Offer carbamazepine\*, leviteracetam or lamotrigine as first-line treatment to children with newly diagnosed focal seizures. Sodium valproate should not be prescribed in females of child bearing age with focal epilepsy unless no reasonable alternative exists. Avoid valproate in children under 3 years if aetiology of epilepsy is unclear.



### Note

Children of South East Asian origin should be screened for HLA-B\*1502 haplotype via the Blood Bank prior to the initiation of carbamazepine - positive children should not receive carbamazepine.



If not seizure free after trial of two ASMs refer to a paediatric neurologist.

# Special considerations for children under 3 years of age

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## Efficacy of ASMs

There is very limited evidence to support any of the current agents for use in infants with seizures. Recent recommendations by the ILAE Commission of Paediatrics gives a strong recommendation for the use of levetiracetam in children of this age group who have focal seizures (Wilmhurst, et al., 2015).



### Special warning

Given potential fatal liver toxicity that can be unmasked by sodium valproate in children under three years of age with certain metabolic disorders (e.g. mitochondrial disorders), sodium valproate should not be used first-line in children in this age group if the aetiology is unclear, until the results of their metabolic screen make any of these disorders unlikely.

## Kinetics of ASMs

There is evidence that infants metabolise ASMs at different rates to older children. This needs to be considered when dosing.

- Carbamazepine – increased clearance
- Phenytoin – increased clearance
- Topiramate – increased clearance
- Levetiracetam – decreased clearance.

## ASM suspensions

This applies to all ages of children requiring a suspension. All suspensions should be formulated by the community pharmacy exactly as recommended on the Emixt website. Specifically clobazam suspension should be prescribed as follows: 1mg/ml suspension as per Emixt recipe.

<https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>

## Metabolic conditions

The ILAE Commission of Paediatrics (Wilmhurst, et al., 2015) recommends that in any infant with medication-resistant seizures or in whom a structural or syndromic cause is not evident, underlying metabolic disease should be considered. Recommended testing includes:

- glucose
- basic haematological screening

- liver function tests including ammonia
- urine analysis
- pH and arterial gases
- plasma electrolytes (sodium (Na), potassium (K), chloride (Cl) for anion gap measurement)
- CSF and plasma lactate
- CSF glucose (paired with blood glucose)
- Serum and CSF amino acid and urine organic acid chromatography or tandem mass spectrometry

**Table 1: Epilepsy types associated with metabolic conditions, with onset in the infantile period**

<b>Epilepsy type</b>	<b>Metabolic condition</b>
Epileptic spasms:	Biotinidase deficiency, Menkes' Disease, organic acidurias, amino acidopathies, mitochondrial respiratory chain diseases.
Early myoclonic epilepsy group:	Consider vitamin-dependent diseases (pyridoxine or pyridoxal-phosphate), amino acid disorders such as non-ketotic hyperglycinaemia, methylene tetrahydrofolate reductase (MTHFR) deficiency, GABA transaminase deficiency, serine deficiency, creatinine deficiency, congenital glutamine deficiency, defects of purine metabolism, sulphite oxidase deficiency, peroxisomal disorders and Carbohydrate-Deficient Glycoprotein (CDG) syndromes, often the aetiology remains unknown.
Epilepsy with myoclonic seizures	Non-ketotic hyperglycinaemia, mitochondrial disorders, GLUT1 deficiency and storage disorders
Absence epilepsy (early onset)	GLUT1 deficiency.
Epilepsy with generalised tonic-clonic seizures:	GLUT1 deficiency, NCL2, other storage disorders, mitochondrial disorders.
Epilepsy with myoclonic-astatic seizures	These can occur in GLUT1 deficiency and NCL2.
Epilepsy with (multi-)focal seizures	Consider GLUT1 deficiency.
Epilepsy partialis continua:	Alpers' Disease, other mitochondrial disorders

Source: ILAE Commission of Paediatrics (Wilmhurst, et al., 2015). Epilepsy types associated with specific metabolic conditions with onset in the infantile period (expert opinion; class 4 studies)

# Special considerations for females with epilepsy

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## ASM therapy

Be aware of the latest data on the risks to the unborn child associated with ASM therapy when prescribing for women and girls of present and future childbearing potential. All ASMs have the potential to harm a fetus.

Discuss with women and girls of childbearing potential (including young girls who are likely to need treatment into their childbearing years), and their parents and/or carers if appropriate, the risks of ASMs causing malformations and neurodevelopmental impairments in an unborn child. Assess the risks and benefits of treatment with individual drugs. There are limited data on risks to the unborn child associated with newer drugs. Specifically discuss the risks of congenital abnormalities and cognitive impairment with the use of sodium valproate to the unborn child, being aware that higher doses of sodium valproate (more than 800 mg/day) and polytherapy, particularly with sodium valproate, are associated with greater risk.

Offer 5mg per day of folic acid to all women and girls on ASMs before any possibility of pregnancy.

Aim for seizure freedom before conception and during pregnancy (particularly for women and girls with GTC seizures) but consider the risk of adverse effects of ASMs and use the lowest effective dose of each ASM, avoiding polytherapy if possible.

✚ See the ACC physician and family information sheets – a link to these is located at:

<https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>

## Contraception in women and girls taking enzyme-inducing ASMs

The progestogen-only pill is not recommended as reliable contraception in women and girls taking enzyme-inducing ASMs.

Information should be given regarding ASMs that impact on the efficacy of the oral contraceptive pill, which can be found at:

<https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>

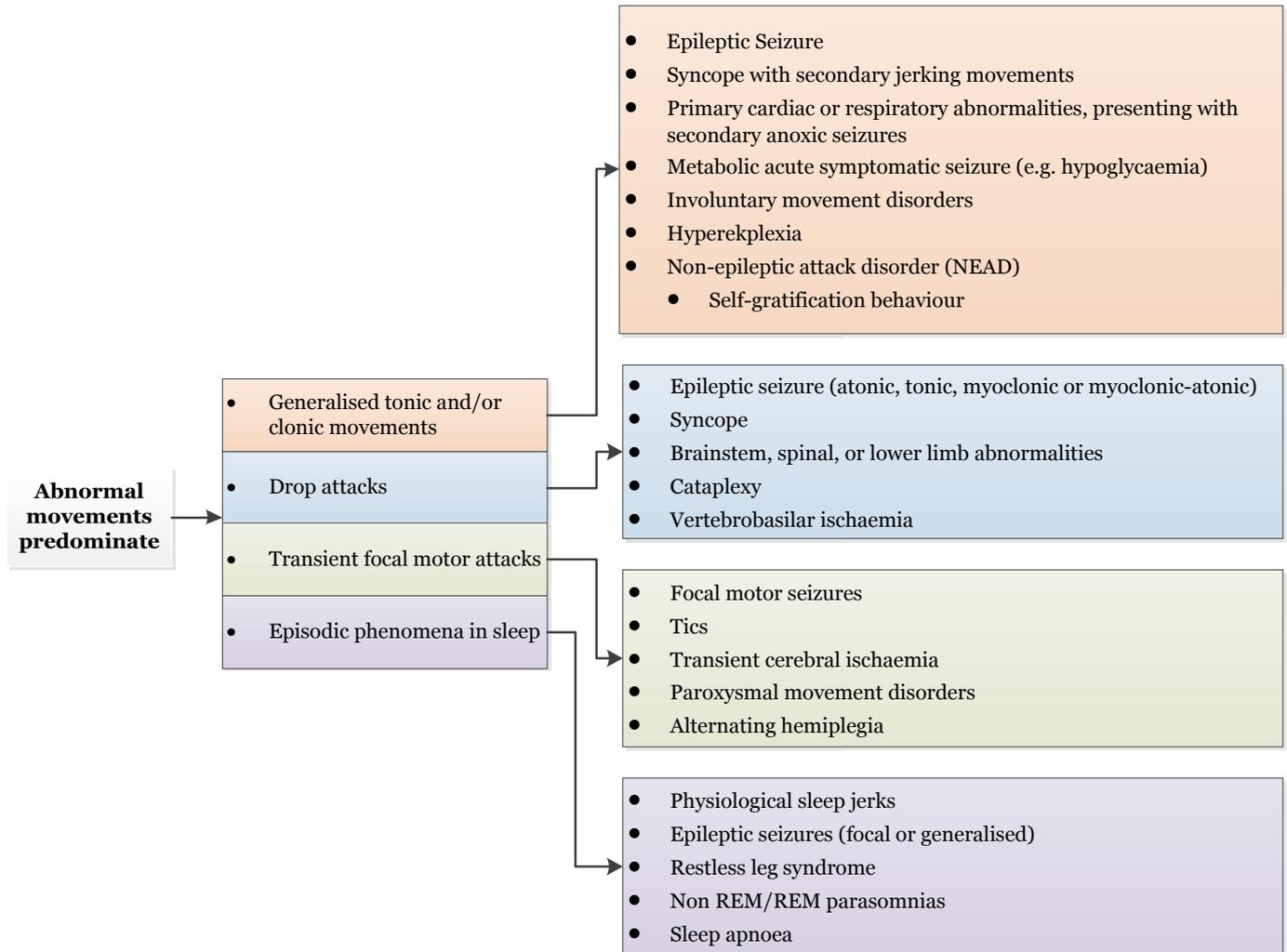
# Pregnancy

Women and girls with epilepsy need accurate information during pregnancy. Discuss the possibility of status epilepticus and sudden unexpected death in epilepsy (SUDEP) with all women and girls who are considering stopping ASM therapy. Information can be found at:

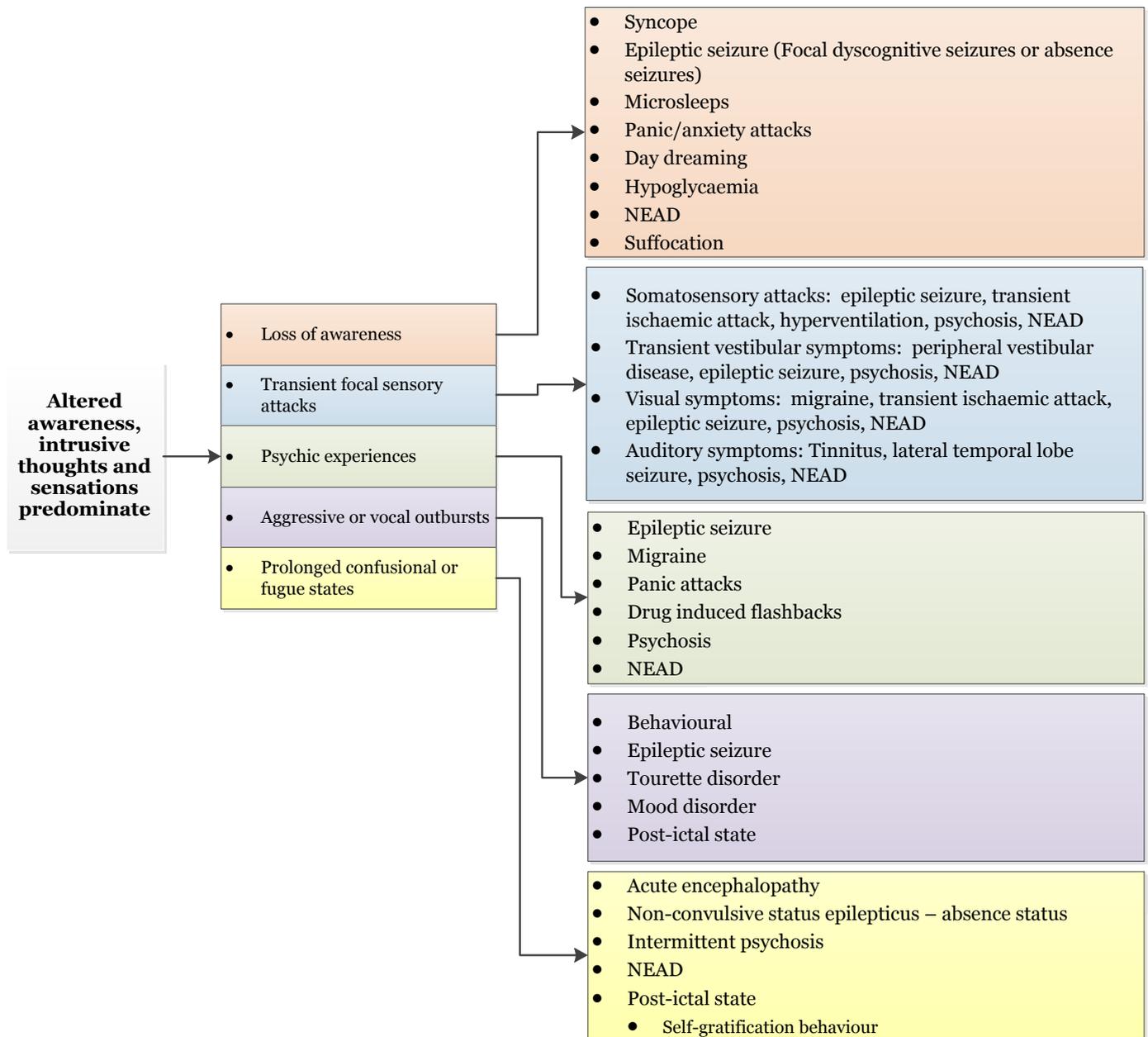
<https://www.starship.org.nz/for-health-professionals/new-zealand-child-and-youth-clinical-networks/paediatric-neurology-clinical-network>

# Differential for paroxysmal event

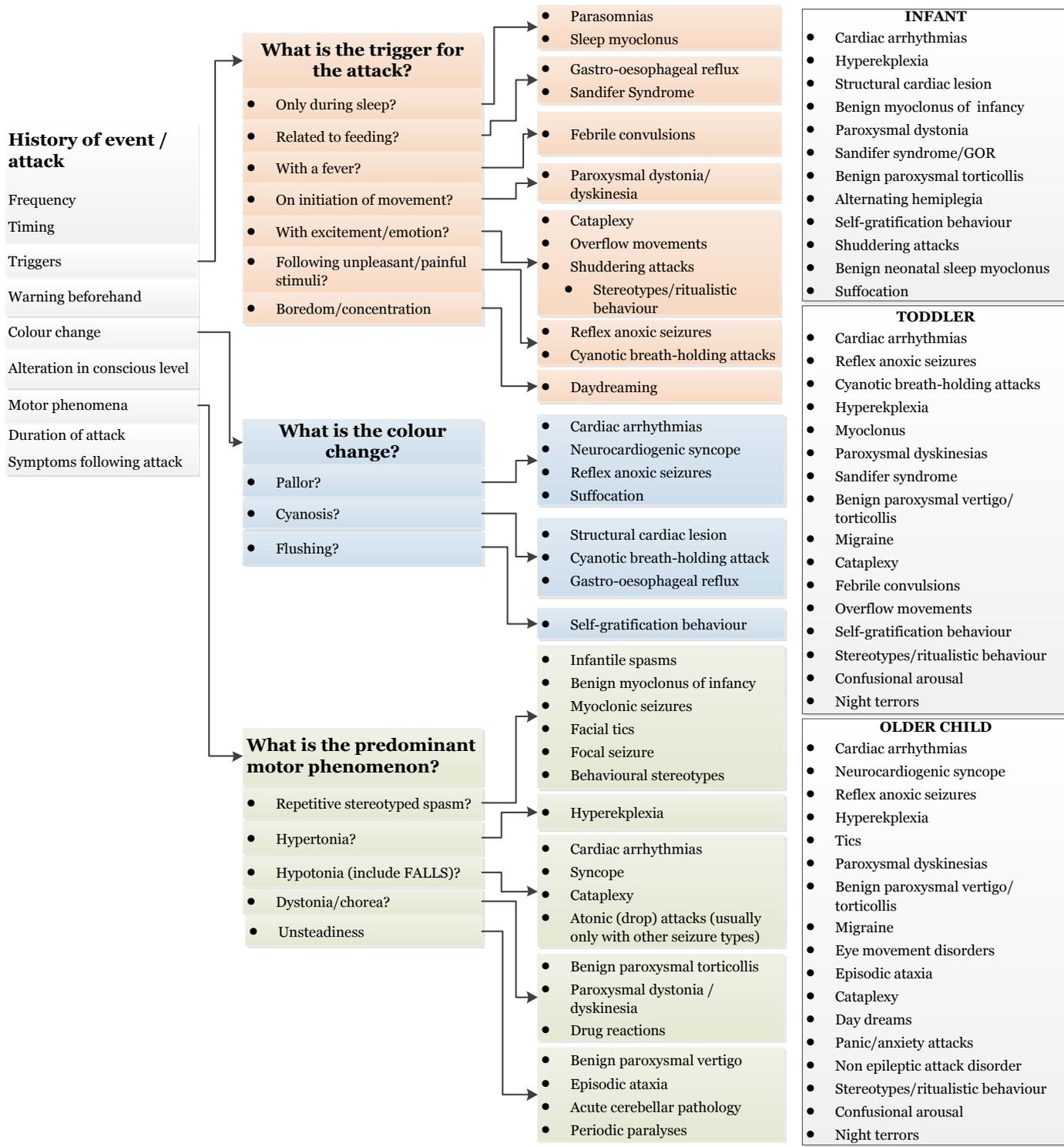
Figure 4: Abnormal movements predominate



**Figure 5: Altered awareness, intrusive thoughts and sensations predominate**



**Figure 6: History of event/attack**



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