BMJ Best Practice

# Generalised seizures in children

Straight to the point of care

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# Summary

Seizures in children may occur as a stand-alone event or may recur (epilepsy).

Aetiology can be structural, genetic, infectious, metabolic, immune, or unknown.

An attempt should be made to identify the type(s) of epilepsy and the epilepsy syndrome by recognising a pattern of seizure types, clinical features, aetiologies, and electroencephalogram characteristics.

Detailed history is of paramount importance in the diagnosis, as key diagnostic factors lie in the history as opposed to ancillary investigations.

Treatment will vary depending on the epilepsy syndrome. Options include anticonvulsant medication, ketogenic diets, vagus nerve stimulation, and surgery, as well as consideration of lifestyle factors.

# Definition

Generalised seizures are understood to originate at some point within the brain and rapidly engage bilaterally distributed networks. This can include both cortical and subcortical structures and may not necessarily involve the entire cortex.[1] [2] The 2017 International League Against Epilepsy (ILAE) classification presents three levels to help guide the clinician: 1) diagnosis of the seizure type; 2) diagnosis of the epilepsy type (focal epilepsy, generalised epilepsy, combined focal and generalised epilepsy, and an unknown group); 3) these two levels help determine the epilepsy syndrome, which is often an electroclinical syndromic diagnosis. Aetiology and comorbidities are taken into account along each step.[1] A detailed ILAE classification and definition of epilepsy syndromes was published in 2022.[3]

Seizures may occur as a stand-alone event. If unprovoked seizures recur, or have a high likelihood of recurrence, the term 'epilepsy' is used. This topic addresses generalised epilepsies. Previous terminology of 'secondarily generalised' seizure (i.e., a focal-onset seizure that spread to involve the rest of the body) has now changed to 'focal to bilateral tonic-clonic seizure'. It is also recognised that if the onset of a seizure is unwitnessed or cannot be described, this would be an 'unknown onset tonic-clonic seizure'.[2]

This topic does not include seizures in neonates.

For information on febrile seizures, see the topic Febrile seizure .

THEORY

# Epidemiology

The epidemiology of childhood seizures usually includes all types of seizures and syndromes; hence, it is difficult to quantify data specifically for generalised seizures. Generalised seizures are overall more common than focal seizures, although one study found that generalised epilepsies and syndromes were more prevalent in children 0-5 years of age, while focal seizures were more prevalent in older children.[4] [5]

The incidence of epilepsy depends on age. Incidence is highest in the first year of life, with reported values of between 81 and 130 per 100,000 per year.[4] Between around 1 and 10 years of age the reported incidence is 40 to 60 per 100,000 per year, with a lower incidence again in adolescence (20 to 25 per 100,000 per year; similar to levels among adults in developed countries).[4] Incidence has not been reported to differ between boys and girls.[4]

Several studies have estimated the prevalence of epilepsy in children: reported values include 3.2 to 5.1 per 1000 in Europe, with values depending on age and country (2005 study); 4.71 per 1000 in Oklahoma (1989); 6.3 per 1000 in the US (2012); and 5.3 per 1000 in Canada (2011). Reported prevalence is generally higher in medium- and low-income countries (especially in rural areas), and among deprived populations in high-income countries.[4]

# Aetiology

Generalised seizures may be genetic, or may be due to an underlying metabolic or immune disease, or less commonly may occur in the presence of a structural abnormality, typically diffuse, of the brain (in which case there may also be focal seizures), or their aetiology may be unknown. The International League Against Epilepsy (ILAE) uses the following aetiological classification system.[1]

Genetic

- Seizures result directly from a known or presumed pathogenic genetic variant. The epilepsies in which a genetic aetiology has been implicated are quite diverse. Although well over 100 epilepsy-associated genes or loci have been identified, in most cases the underlying genes are not yet known. Examples of genetic epilepsies include Dravet syndrome and genetic epilepsy with febrile seizures plus (GEFS +). There is usually not a specific inheritance pattern, but rather a complex inheritance, often with age-dependent penetrance.[6]
- The term 'genetic generalised epilepsies' is used for the broad group of epilepsies with generalised seizure types and generalised spike-wave, based on a presumed genetic aetiology. This includes the subgroup of 'idiopathic generalised epilepsies', which refers to the four syndromes of childhood absence epilepsy, juvenile myoclonic epilepsy, juvenile absence epilepsy, and epilepsy with generalised tonic-clonic seizures alone, which are the most common syndromes within the generalised genetic epilepsies.[1] [3] [7]

Structural

- Refers to abnormalities visible on structural neuroimaging, where the electroclinical assessment together with the imaging findings lead to a reasonable inference that the imaging abnormality is the likely cause of the patient's seizures. Structural aetiologies may be acquired (e.g., stroke, trauma, and infection), or genetic (e.g., many malformations of cortical development). When a structural aetiology has a well-defined genetic basis, both aetiological terms (genetic and structural) can be used.[1] Identification of a subtle structural lesion requires appropriate magnetic resonance imaging (MRI) studies using specific epilepsy protocols.

Metabolic

- Generalised seizures can be due to a known or suspected metabolic disorder or neurodegenerative disorder (epilepsy is then part of a generalised encephalopathy).

Immune

- Seizures result directly from an immune disorder in which seizures are the core symptom of the disorder. An immune aetiology should be suspected when there is evidence of autoimmune-mediated central nervous system inflammation. Examples include anti-NMDA (N-methyl-D-aspartate) receptor encephalitis and anti-LGI1 encephalitis (although these are more commonly associated with focal seizures).

Infectious

- Seizures result directly from a known infection in which seizures are the core symptom of the disorder. The most common aetiology worldwide is where epilepsy occurs as a result of an infection. An infectious aetiology refers to a patient with epilepsy, rather than with seizures occurring in the setting of acute infection such as meningitis or encephalitis. Examples include neurocysticercosis, tuberculosis, HIV, cerebral malaria, subacute sclerosing panencephalitis, cerebral toxoplasmosis, and congenital infections such as Zika virus and cytomegalovirus.

Unknown

- When the generalised epilepsy cannot be classified as one of the four idiopathic generalised epilepsy syndromes or evidence is lacking for a genetic basis, the epilepsy can be classified as having an unknown basis.

# Pathophysiology

Our current understanding of the pathophysiology is rather limited. During an epileptic seizure, an alteration in central nervous system function leads to a paroxysm of electrical discharges in the cortex or brainstem. Excitatory and inhibitory neurotransmitters play a role in the development of seizure discharges. In general, increased neuronal excitability and synchronicity is thought to be responsible for seizure initiation and propagation. Change in the synaptic function and intrinsic properties of neurons may be the cause of hyper-excitability. This in turn can be the result of a change in balance between the glutamate and gamma-aminobutyric acid (GABA) neurotransmitter systems. Catecholaminergic neurotransmitter systems and opioid peptides are also shown to play a role in epileptogenesis. A variety of genetic and structural abnormalities can contribute to groups of neurons developing this state.

Increasingly, the role of functional networks as opposed to structural anatomical networks is seen as relevant, with epilepsies being perceived as 'a disorder of cortical network organisation'.[8] A model involving circuitry of cortical and thalamic neurons has been suggested for absence epilepsy. Within this circuit there are 'fast-spiking neurons' and interconnecting inhibitory neurons, the activity of both being modulated by GABA.[9] In addition to this thalamo-cortical network, other models include a limbic, a neocortical, and a brainstem network.

# Classification

## ILAE seizure type[2]

The International League Against Epilepsy (ILAE) system classifies generalised-onset seizures into the following types based on motor or non-motor clinical manifestations:

- Non-motor: absence; interruption in the child's activities, often with a blank stare or inattention (i.e., behavioural arrest)
    - Typical
    - Atypical
    - Myoclonic absence
    - Eyelid myoclonia
- Motor:
    - Clonic: rhythmic, muscular jerking movements with or without impaired consciousness
    - Tonic: tonic extension or flexion of the extremities
    - Tonic-clonic: this usually starts with a tonic phase and the patient becoming unconscious, possibly falling to the ground, and extension or flexion of extremities. It may be preceded by aura. The clonic phase consists of often violent muscle contractions resulting in apparent shaking.
    - Myoclonic: brief, arrhythmic, muscular jerking movements involving one or a group of muscles
    - Myoclonic-atonic
    - Myoclonic-tonic-clonic
    - Atonic: brief loss of muscle tone causing what are known as 'drop attacks', where the patient falls to the ground
    - Epileptic spasms

## ILAE aetiological classification[1]

The ILAE classifies seizures as being due to genetic, structural, immune, infectious, metabolic, or unknown aetiology. For further details, see Aetiology .

## Epilepsy syndromes[3]

In 2022 the ILAE published a classification and definition of epilepsy syndromes. An epilepsy syndrome is defined as "a characteristic cluster of clinical and electroencephalographic features, often supported by specific etiological findings (structural, genetic, metabolic, immune, and infectious)".[3]

In clinical practice, the clinical features including age of onset of seizures, other signs, symptoms, and electroencephalogram findings help make an electroclinical syndromic diagnosis. Different syndromes have different natural histories, and at times the syndromic diagnosis can guide treatment. Important features to identify include how responsive seizures are to treatment and the degree of developmental impairment.

The previous term 'symptomatic generalised epilepsy', often used to refer to epilepsy with rapid bilateral network involvement due to an underlying cause, is now replaced by the term 'developmental and/or epileptic encephalopathy', which can consist of generalised, focal, or a combination of both types of seizures. The concept of epileptic encephalopathy implies that the epilepsy is directly impacting development, causing cognitive and behavioural plateau and regression. In developmental and epileptic encephalopathies, the specific genetic, structural, or other acquired aetiologies of the epilepsy are associated with developmental impairment, which is then further impacted by the epilepsy.[1]

The following are the more common epilepsy syndromes (i.e., not an exhaustive list) with predominantly generalised seizures that are recognised in childhood, sub-divided by typical age of onset as defined by the ILAE.[3]

Onset in infancy (1 month to 2 years)

- Genetic epilepsy with febrile seizures plus (GEFS+) spectrum
- Myoclonic epilepsy in infancy (MEI)
- Early infantile developmental and epileptic encephalopathy (EIDEE) (includes Ohtahara syndrome)
- Infantile epileptic spasms syndrome (IESS) (includes West syndrome)
- Dravet syndrome

Onset in childhood (usually 2-12 years)

- Epilepsy with myoclonic-atonic seizures (EMAtS)
- Lennox-Gastaut syndrome (LGS)
- Childhood absence epilepsy (CAE)
- Epilepsy with myoclonic absence (EMA)
- Epilepsy with eyelid myoclonia (EEM)

Onset at a variable age (usually 10-14 years)

- Juvenile myoclonic epilepsy (JME)
- Juvenile absence epilepsy (JAE)
- Epilepsy with generalised tonic-clonic seizures alone (GTCA)

# Case history

## Case history #1

A 10-year-old girl presents after having had a generalised tonic-clonic seizure while at school the previous day. It lasted approximately 2 minutes and she was incontinent of urine during the episode. Afterwards she complained of headache and feeling tired. She had been well prior to this episode and there is no family history of epilepsy. General physical examination including neurological assessment on the day after the seizure were both normal. An ECG was done, which was normal and showed a normal QTc interval.

## Case history #2

A 15-year-old boy presents with a history of having had two seizures. He is healthy and has no relevant past medical history. There is no family history of epilepsy. Both episodes happened early in the morning and were self-limiting. Jerking of the whole body and all four limbs lasted <5 minutes, and he was sleepy for several hours after the episodes. His general examinations, including blood pressure, a random blood sugar, and an ECG, were normal.

## Other presentations

While generalised tonic-clonic seizures are easily recognisable, in some instances a generalised seizure is not obvious. Tonic-clonic seizures that occur exclusively at night may only come to light when the patient shares a bedroom or if the accompanying noise wakes up a family member. Absence seizures

are characterised by a sudden interruption in the child's activities, often with a blank stare or inattention. Atonic seizures are characterised by a brief loss of muscle tone causing what used to be referred to as 'drop attacks', whereby the patient suddenly and limply falls to the ground. Myoclonic seizures are characterised by brief, arrhythmic muscular jerking movements. Clonic seizures consist of rhythmic, muscular jerking movements with or without impaired consciousness. Tonic seizures consist of tonic extension or flexion of the extremities.

# Approach

A detailed history is of paramount importance, as epileptic seizures are often not witnessed by a physician. A description of the seizure onset is key (to help categorise as focal-onset or generalised-onset seizure), as well as additional information such as: the setting, any possible provoking factors, warning signs that the child or young person may be able to recount, and any postictal phenomena. An electroencephalogram (EEG) is used to help determine the specific epilepsy syndrome and identify features such as photosensitivity.[18] [19] Standard laboratory tests such as fulll blood count and basic metabolic panel (blood sugar, calcium, magnesium) are not routinely indicated, but may be requested initially to exclude any underlying causes. Brain imaging may be indicated if the onset of the seizure has not been witnessed or if there is suggestion of a focal onset; however, in most cases of generalised epilepsies with a clear electroclinical syndromic diagnosis, brain imaging is not indicated. Genetic testing is recommended if certain epilepsy syndromes are suspected.

The ILAE Commission on Classification and Terminology has developed an online diagnostic manual of the epilepsies to assist clinicians to diagnose seizure type(s), diagnose epilepsy syndromes, and define the aetiology of the epilepsy. [ILAE: EpilepsyDiagnosis.org] (https://www.epilepsydiagnosis.org)

## History

History can be elicited from the parents or any eyewitnesses. Family history of seizures or epilepsy, past medical history, birth history, and the child's developmental history should be noted.

It is important to go through the events in chronological order, exploring the circumstances of the seizure, what the child was doing at the time, possible triggers (e.g., light, noise, sleep deprivation, fatigue, emotional state), presence of aura or other warnings (e.g., déjà vu, dizziness, altered vision), and how the seizures started and what they looked like. Video recording an episode or capturing the event on a smartphone is very useful to the clinician. Alternatively, demonstrating some of the movements or asking any witnesses to mimic what they saw is usually extremely helpful in determining the type of seizure (i.e., myoclonic, atonic, tonic and/or clonic, or absence). Traditionally the following have been thought to signify an epileptic seizure: specific movements; tone; state of consciousness; presence of incontinence, tongue biting, or eye movements, as well as how the seizure ended and if there were any signs/symptoms (e.g., sleepiness, headache, amnesia, confusion) in the post-ictal state. However, these on their own do not equate to a person having had an epileptic seizure.

Seizure types

Characteristics of seizure types include:[2]

- Absence: impairment (usually brief) of awareness, which may be associated with motor arrest or with stereotyped movements or automatisms. It is important to differentiate between the two types of absence seizure, as they occur in different epileptic syndromes:
    - Typical absence seizure: behavioural arrest or staring, lasting 5-10 seconds, interrupting otherwise normal activity; can be hyperventilation-induced
    - Atypical absence seizure: less distinct beginning and end; not usually precipitated by hyperventilation.
- Myoclonic: brief, arrhythmic muscular jerking movements.
- Clonic: rhythmic, muscular jerking movements with or without impaired consciousness.
- Tonic: tonic extension or flexion of the extremities.

- Tonic-clonic: tonic phase involves the patient falling unconscious, possibly falling to the ground, and extension or flexion of extremities, and may be preceded by aura; clonic phase consists of usually violent muscle contractions and shaking.
- Atonic: brief loss of muscle tone causing what are known as 'drop attacks', where the patient falls to the ground.

Length of seizures may vary from one event to another in the same person, but length can also be a specific characteristic of a seizure. For example, absence seizures typically last for up to 20 seconds, and a longer duration is so exceptional that it would warrant questioning the diagnosis.[20] Most generalised tonic-clonic seizures last <5 minutes. Differentiating between these and generalised tonic-clonic seizures that last longer is not helpful diagnostically, but informs immediate management decisions.

Sometimes seizures can be induced by light. This is called photosensitivity and is a useful diagnostic characteristic. The following syndromes are known to be photosensitive: epilepsy with eyelid myoclonia, juvenile myoclonic epilepsy, epilepsy with generalised tonic-clonic seizures alone, Dravet syndrome, and progressive myoclonic epilepsies.[21] [22]

## Physical examination

After an unprovoked seizure, the possibility of an underlying disorder should be considered during the clinical assessment. The physician should look for neurocutaneous signs, as conditions with these signs can manifest with seizures, including tuberous sclerosis complex (i.e., depigmented macules, shagreen patches, periungual fibromas, adenoma sebaceum, and ash-leaf macules), neurofibromatosis type 1 (i.e., cafe au lait spots, axillary and inguinal freckling, and plexiform neurofibromas), and Sturge-Weber syndrome (i.e., port wine-coloured haemangiomas on the face or trunk).[12]

Full neurological examination is an important part of the evaluation. Blood pressure, head circumference measurement, and an ECG is required for any child who has had a generalised seizure. In the majority of patients with recurrent generalised seizures there are no abnormalities.

## Electroencephalogram (EEG)

EEG is a standard investigation for diagnosis of epilepsy.[23] Epileptic discharges may be seen on the inter-ictal recording, and abnormal rhythms can be characteristic for a specific epilepsy syndrome.[18] [19] About 5% of children without epilepsy have non-specific abnormalities on EEG, and up to 40% of children with epilepsy have normal inter-ictal EEGs. Therefore, EEG complements history, physical, and other evaluation techniques. A normal inter-ictal EEG does not exclude a diagnosis of epilepsy. Epileptiform activity in a combined wake and sleep recording increases the probability that the diagnosis of epilepsy is the correct one from 0.17 (for children without these abnormalities) to 0.95.[24]

Hyperventilation, photic stimulation, and sleep deprivation may be used to provoke seizures as part of the EEG investigation or to enhance EEG abnormalities. For childhood absence epilepsy, inducing a seizure in the clinic by asking the child to over-breathe for up to 3 minutes is a useful diagnostic tool, as it will result in an absence seizure in 90% of children with absence epilepsy.[20]

A video EEG may be useful. It is used to determine whether the clinically observed seizures are epileptiform in nature. It can also help to characterise the seizures better and therefore clarify the diagnosis. Some studies suggest that an EEG is useful in predicting the risk of seizure recurrence in children and adolescents.[25] [26]

## Electrocardiogram (ECG)

An ECG should be performed for all children presenting with a first seizure to exclude cardiac causes of clinical events, primarily long QT syndrome.[27] [28] Other possible causes include Brugada syndrome and possible arrhythmias. A cardiologist should be consulted if there is doubt or if there is a family history of early unexplained death.

## Neuroimaging

The combination of typical EEG findings that correlate with the clinical picture can often be diagnostic. However, in cases where the diagnosis is in doubt or a secondary cause is suspected, magnetic resonance imaging (MRI) is the definitive imaging technique in children, as it does not involve ionising radiation and the images give more detail than computed tomography (CT) scans.

CT has a role in acute investigation for children with a recent history of a seizure and in whom an intracerebral bleed needs to be ruled out. It is also used when there are concerns about a space-occupying lesion and an MRI is not available.[23] [29]

Functional MRI may be used for pre-surgical mapping.[30]

## Laboratory investigations

These are not routinely indicated for patients with recurrent seizures. However, blood glucose level, basic metabolic panel, and a full blood count may be considered in children with suspected provoking factors such as hypoglycaemia, electrolyte abnormalities, metabolic disorders, or infection. Blood glucose measurement is an obligatory part of evaluation for any child with decreased consciousness level. It is recommended that these tests are ordered at least once for all patients with recurrent seizures.

## Genetic testing

Genetic testing is recommended for children with suspected Dravet syndrome. It should also be considered for suspected developmental and epileptic encephalopathies (including suspected early infantile developmental and epileptic encephalopathy, infantile epileptic spasm syndrome, and Lennox-Gastaut syndrome), or if structural abnormalities suggest a genetic cause.[21] [31] [32][33]

## Diagnosis of specific epilepsy syndromes

Patient history (including seizure types), EEG, physical examination, and complementary diagnostic information can help classify epilepsy into specific electroclinical epilepsy syndromes. Some syndromes will have a normal EEG, especially at initial presentation, so history and presentation are also vital. Identifying epilepsy syndromes provides guidance on management, outcomes, comorbidities, and potential additional evaluations. The patient's age may also guide diagnosis, since the incidence of specific syndromes peaks during particular age ranges.[1]

Onset in infancy (age 1 month to 2 years)[31]

Early infantile developmental and epileptic encephalopathy (EIDEE; includes Ohtahara syndrome):

- Onset is usually by age 3 months (adjusted for prematurity).
- Tonic and/or myoclonic seizures are typical, but other seizure types may occur.
- EEG may show burst-suppression, multifocal spikes/spike-waves/sharp-waves with or without slowing, discontinuity, and/or diffuse slowing. The burst-suppression pattern comprises high-voltage bursts of mixed spikes, and sharp and slow waves lasting 1-5 seconds, alternating with

periods of marked suppression lasting 3-10 seconds, and may be seen when the patient is awake or asleep. De-synchronisation is seen during tonic spasms.
- Abnormal neurological behaviour or development may be present before onset of seizures (but this may be difficult to assess).
- Causative pathogenic gene variants can be identified in over half of patients.

Infantile epileptic spasms syndrome (IESS):

- Onset of epileptic spasms is usually between 1 and 24 months of age (peak 3-12 months), but may be later.
- Characterised by flexor, extensor or mixed epileptic spasms, which often occur in clusters.
- EEG: hypsarrhythmia (asynchronous asymmetrical spikes and slow waves) is usually, but not always, seen on inter-ictal recordings.
- Development may or may not be normal before onset, but developmental slowing, arrest, or regression is seen after onset.
- A sub-group with the triad of infantile spasms, developmental stagnation or regression, and hypsarrhythmia on EEG is defined as West syndrome.
- Many pathogenic gene variants have been associated with IESS.

Myoclonic epilepsy in infancy (MEI):

- Onset is usually between ages 4 months and 3 years (peak 6-18 months).
- Characterised by myoclonic seizures that occur multiple times a day both during sleep and when awake. They may be triggered by noise, startle, touch, or (less commonly) photic stimulation. The seizures may be brief and singular, or occur in clusters.
- EEG: background is normal, but generalised poly-spike or spike-and-slow-wave discharges are seen during myoclonic seizures.
- Development is usually normal before seizure onset. A majority of patients show normal developmental outcome, but mild intellectual disability or behavioural problems may be seen. Moderate to severe intellectual disability is rare.

Dravet syndrome:

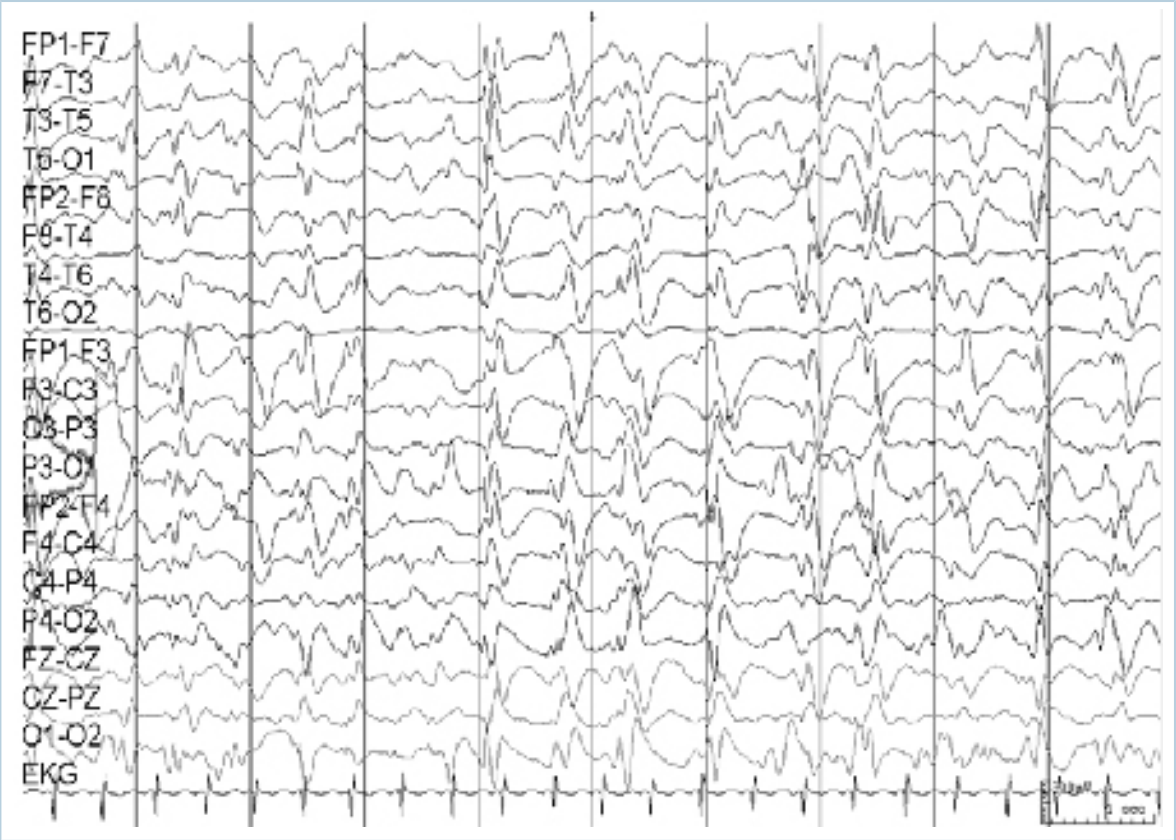
- Onset by age 1 year, with characteristic prolonged, febrile and afebrile, focal clonic (usually hemiclonic), or generalised clonic seizures.
- Other seizure types (e.g., myoclonic, atonic, tonic-clonic, and/or atypical absence seizures) may appear between the ages of 1 and 4 years.
- EEG is initially normal. After age 2 years, slowing is typical, and inter-ictal discharges are often focal, multifocal, and generalised. Ictal recordings depend on seizure type.
- Children typically have normal development before onset of seizures. Developmental plateau and other neurological abnormalities, such as ataxia, often present during the second year of life.
- Frequently, there is a family history of febrile seizures. A pathogenic variant in the SCN1A gene is present in over 80% of cases.

Onset in childhood (age 2-12 years)[7] [32]

Epilepsy with myoclonic-atonic seizures (EMAtS; formerly known as Doose syndrome):

- Should be considered in pre-school children presenting with generalised seizures (generalised tonic-clonic, myoclonic, absence) who develop myoclonic-atonic seizures.
- During a myoclonic-atonic seizure the child has a brief jerk (myoclonus), sometimes accompanied by an audible grunt, then abruptly loses muscle control and may fall to the ground. There is an associated loss of consciousness, but this is very brief (<3 seconds).

- EEG is initially normal, although more commonly the inter-ictal recording shows some slowing with excess of theta activity. Appearance of the ictal EEG depends on the type of seizure: absences are associated with slow spike and waves, tonic-clonic seizures are associated with generalised 10- to 15-Hz poly-spikes, and myoclonic and atonic seizures are associated with irregular generalised spike-and-wave discharges.



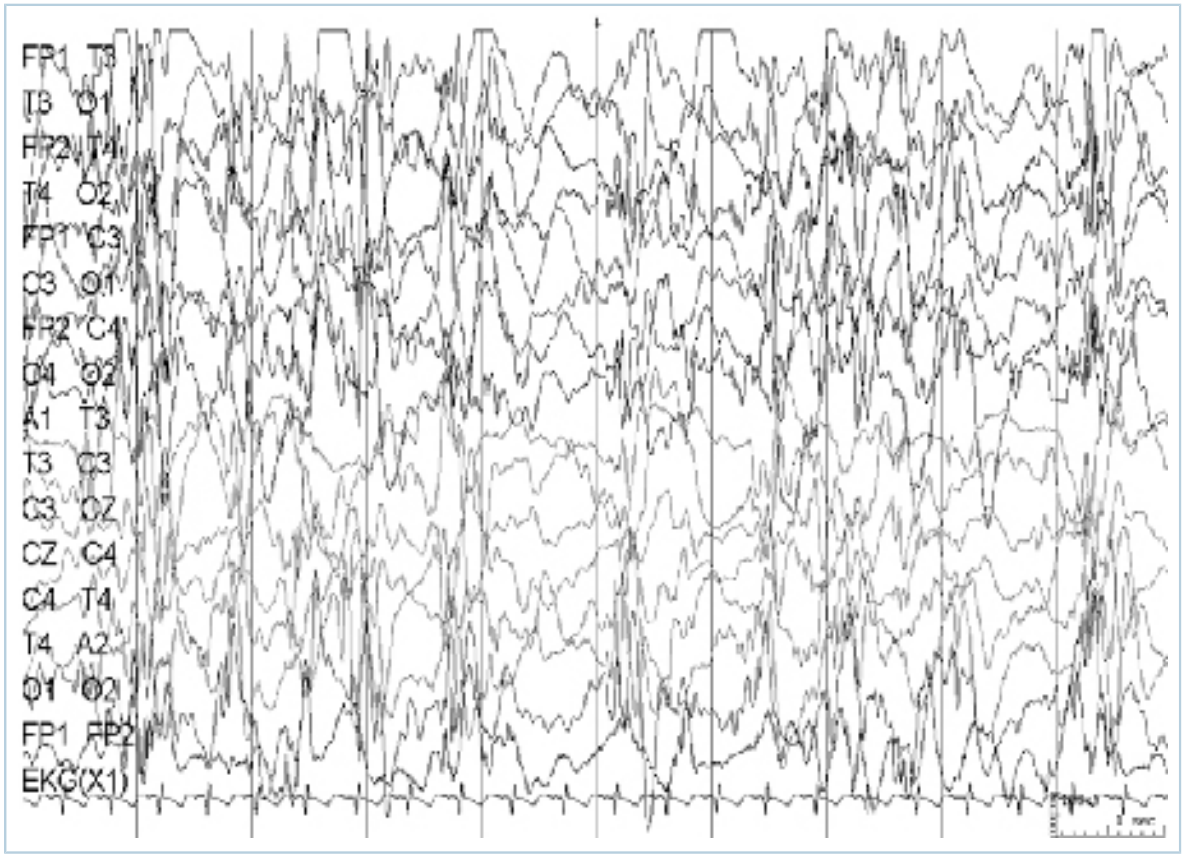

*Electroencephalogram (EEG): epilepsy with myoclonic-atonic seizures*

*Courtesy of Professor Eric Kossoff; used with permission*

- Most affected children have normal development before the onset of epilepsy, but about 50% go on to develop learning difficulties or mild/moderate intellectual disability.[34]

Lennox-Gastaut syndrome (LGS):

- Onset is usually between ages 18 months and 8 years, with peak onset at 3-5 years.
- The presence of tonic seizures lasting from 3 seconds to 2 minutes is mandatory for diagnosis.
- Many other types of seizure may occur, including tonic-clonic, atonic, myoclonic, focal, and atypical absence.
- Many patients show only some of the characteristic features over a certain period of time; clinical manifestations are often not all present in a given person.
- EEG: abnormal inter-ictal EEG is a hallmark of this syndrome, showing diffuse, slow (<2.5 Hz) spike-and-wave complexes and generalised paroxysmal fast activity.




*Electroencephalogram (EEG): Lennox-Gastaut syndrome*

*Courtesy of Professor Eric Kossoff; used with permission*

- Most children have developmental delay.
- Up to 75% of patients have recurrent episodes of non-convulsive status epilepticus, which can be difficult to recognise and treat.
- Pathogenic variants in many genes, as well as a range of chromosomal abnormalities and copy number variants, have been associated with LGS.

Epilepsy with myoclonic absence (EMA):

- Onset is typically around age 7 years (range 1-12 years).
- Myoclonic absence seizures are the defining type of seizure; these last up to 1 minute and occur multiple times per day.
- Tonic-clonic, clonic, atonic, or typical absence seizures may also occur.
- Ictal EEG shows bilateral synchronous 3-Hz spike-wave discharges associated with 3-Hz myoclonic bursts; inter-ictal EEG has normal background activity, but up to 30% of patients have superimposed generalised spike-wave discharges.
- Patients may have developmental impairment at presentation, and some will subsequently have a degree of intellectual disability.

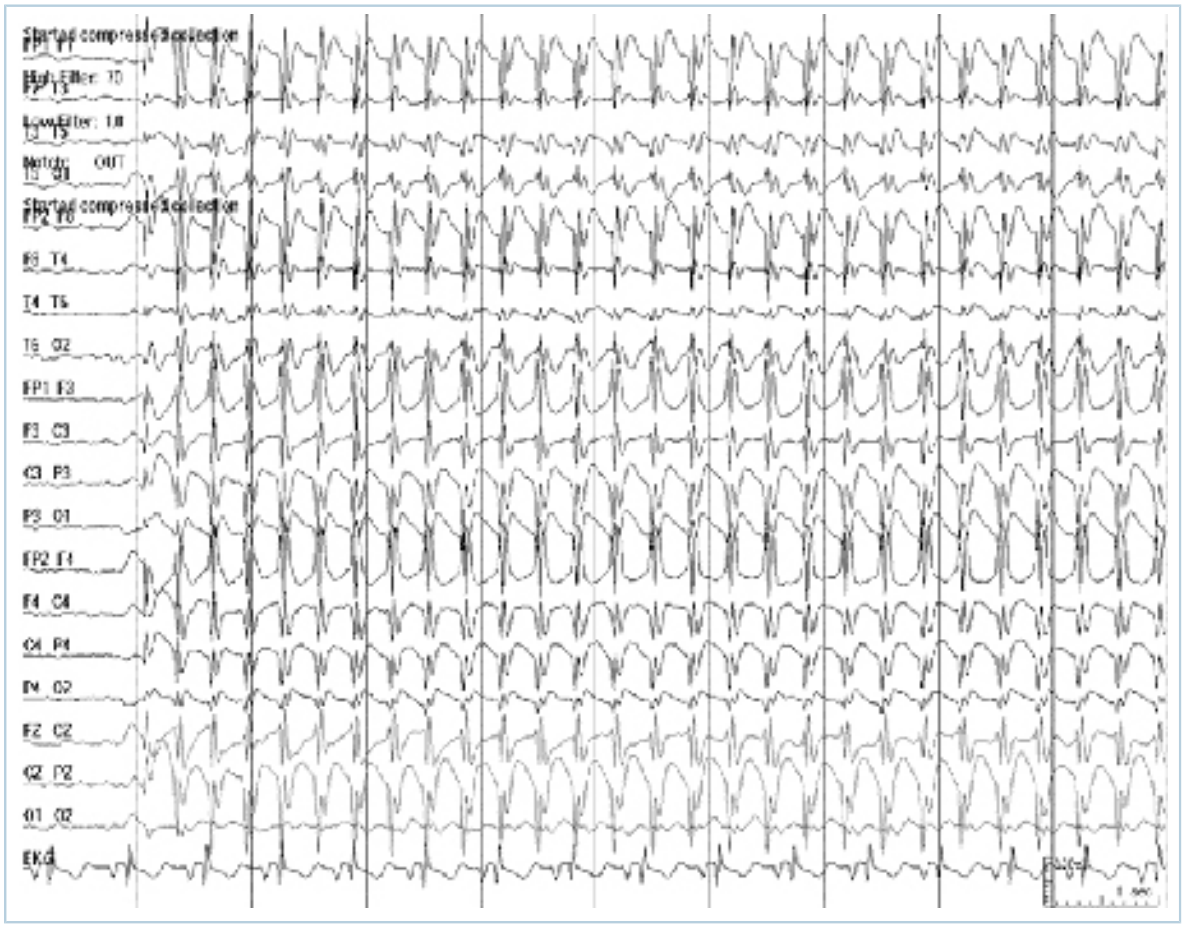
Epilepsy with eyelid myoclonia (EEM):

- Peak age at onset is between 6 and 8 years (range 2-14 years).
- The most typical feature is eyelid myoclonia that occurs frequently with eye closure, may be provoked by light (photic induction), and is often associated with brief absence seizure. Seizures last only a few seconds but occur many times per day.
- Other seizure types that may be seen include generalised tonic-clonic, myoclonic, and typical absence seizures.

- EEG: on eye closure (or photic stimulation), brief discharges of fast activities are seen; a typical pattern is 3- to 6-Hz poly-spike waves.
- Development is often normal, but intellectual disability may be seen, and is more likely in patients with prominent photic induction.

Childhood absence epilepsy (CAE):

- Onset is typically between ages 4 and 10 years (range 2-13 years).
- Typical absence seizures are the predominant seizure type.
- Rarely, generalised tonic-clonic seizures can occur.
- EEG background is normal, with paroxysms of 3-Hz generalised spike-wave. The characteristic pattern of the ictal recording is regular 3-Hz ictal generalised and symmetrical 3-Hz spike-wave.



*Electroencephalogram (EEG): childhood absence epilepsy; shows typical 3 per second spike-and-wave pattern*

*Courtesy of Professor Eric Kossoff; used with permission*

- Development is typically normal.

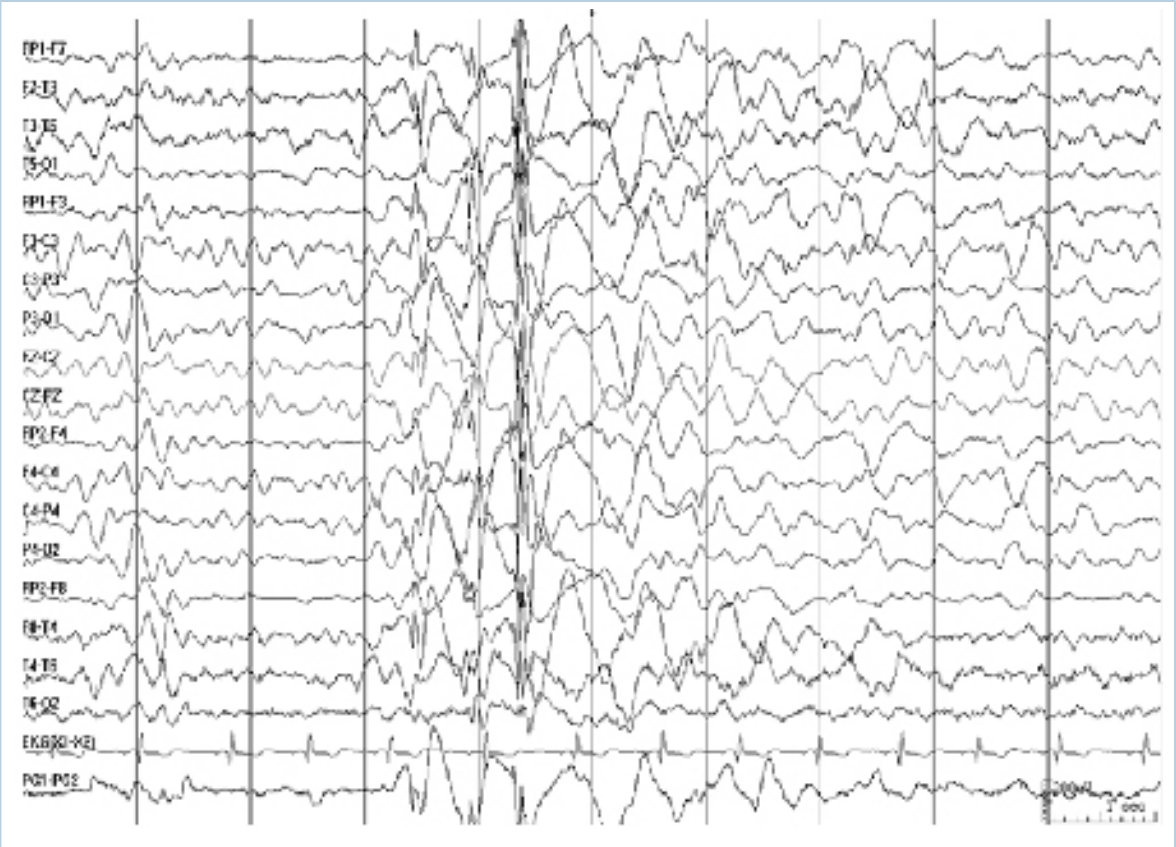
Onset at a variable age

Onset of these syndromes commonly occurs in late childhood and adolescence.[7] Development is typically normal. Common comorbidities include mood disorders, ADHD, and learning disabilities.

Juvenile myoclonic epilepsy (JME):

- Typical age at onset is between 10 and 24 years (range 8-40 years).
- Myoclonic seizures are mandatory for diagnosis; they may be unilateral or bilateral, and occur almost exclusively in the morning and mainly in the upper limbs.

- Generalised tonic-clonic seizures also occur in most patients, and absence seizures in about one third of cases.
- Inter-ictal EEG shows 3.5- to 6-Hz spike- and poly-spike waves; most pronounced during sleep and drowsiness; rapid spikes followed by irregular slow waves are seen during myoclonus.



*Electroencephalogram (EEG): juvenile myoclonic epilepsy*

*Courtesy of Professor Eric Kossoff; used with permission*

Juvenile absence epilepsy (JAE):

- Typical age at onset is between 9 and 13 years (range 8-20 years).
- The predominant seizure type is absence seizure. Absences tend to be longer and less frequent than the absences of childhood absence epilepsy, and loss of awareness is often less complete.
- Generalised tonic-clonic seizures also occur in most patients.
- Ictal EEG shows 3- to 5.5-Hz generalised spike-and-slow-wave discharges; inter-ictal EEG is usually normal.

Epilepsy with generalised tonic-clonic seizures alone (GTCA):

- Typical age at onset is between 10 and 25 years (range 5-40 years).
- Generalised tonic-clonic seizures are mandatory, and no other seizure types occur. Seizures often occur within 2 hours of waking, and are typically infrequent.
- Inter-ictal EEG shows 3- to 5.5-Hz spike- and/or poly-spike-wave discharges.

# History and exam

## Key diagnostic factors

### presence of risk factors (common)

- Key risk factors include genetic predisposition or family history, antenatal or perinatal insults, metabolic/neurodegenerative disorders, traumatic brain injury, structural abnormalities of the central nervous system, history of febrile seizures, and neurocutaneous syndromes.

### staring spells or inattention (common)

- Usual characteristics of absence seizures.
- Brief impairment of consciousness that may be associated with motor arrest or with stereotyped movements. Often first noted by teachers.
- It is important to differentiate between the two types of absence seizure, as they occur in different epileptic syndromes.
- Typical absence seizure: behavioural arrest or staring, lasting 5-10 seconds, interrupting otherwise normal activity. Can be hyperventilation-induced.
- Atypical absence seizure: less distinct beginning and end, not usually precipitated by hyperventilation.
- May occur in the following syndromes: Dravet syndrome, epilepsy with myoclonic-atonic seizures, Lennox-Gastaut syndrome, childhood absence epilepsy, epilepsy with myoclonic absence, juvenile myoclonic epilepsy, and juvenile absence epilepsy.

### tonic-clonic seizures (common)

- Tonic phase involves the patient falling unconscious, possibly falling to the ground, and extension or flexion of extremities. May be preceded by aura. Clonic phase consists of usually violent muscle contractions, shaking, or vibrating. Eyes may roll back in head, tongue may be bitten, and incontinence may occur. Often followed by post-ictal phenomena.
- May occur in the following syndromes: Dravet syndrome, epilepsy with myoclonic-atonic seizures, Lennox-Gastaut syndrome, epilepsy with myoclonic absence, epilepsy with eyelid myoclonia, juvenile myoclonic epilepsy, and epilepsy with generalised tonic-clonic seizures alone.
- Clonic or tonic seizures may also occur in isolation.
- Early infantile developmental and epileptic encephalopathy usually presents with tonic spasm, and seizures often come in clusters.

### brief, arrhythmic muscular jerking movements (common)

- Typical characteristics of myoclonic seizures.
- Dominant seizure type in early infantile developmental and epileptic encephalopathy, which can also be associated with tonic spasms or focal motor seizures.
- May also occur in the following syndromes: Dravet syndrome, epilepsy with myoclonic-atonic seizures, Lennox-Gastaut syndrome, epilepsy with myoclonic absence, epilepsy with eyelid myoclonia, juvenile myoclonic epilepsy, and juvenile absence epilepsy.

### eyes rolling back in head (common)

- Often observers will see the patient's eyes rolling back in the head during tonic-clonic seizures.

### intercurrent illness (common)

- Many people who have recurrent seizures will experience increased frequency of seizures at times of intercurrent minor illness, especially if associated with increased temperature.

### unexplained falls (uncommon)

- Brief loss of muscle tone followed by falling episodes is a typical characteristic of atonic seizures.
- May occur in the following syndromes: epilepsy with myoclonic-atonic seizures, Lennox-Gastaut syndrome, and epilepsy with myoclonic absence.

## Other diagnostic factors

### incontinence (common)

- Urinary or faecal incontinence may occur during tonic-clonic seizures.

### tongue biting (common)

- Patient may bite tongue during tonic-clonic seizures.

### post-ictal phenomena (common)

- Some patients may experience post-ictal phenomena such as sleepiness, headaches, amnesia, or confusion.
- Usually occurs only with generalised tonic and/or clonic seizures.

### precipitated by fatigue or lack of sleep (common)

- Fatigue may increase likelihood of seizures in a person with recurrent seizures.
- Lack of sleep is a well-known precipitating factor for seizures in juvenile myoclonic epilepsy and in epilepsy with generalised tonic-clonic seizures only.[7]

### precipitated by light or noise (common)

- Sometimes seizures can be induced by light. The following syndromes are known to be photosensitive: epilepsy with eyelid myoclonia, juvenile myoclonic epilepsy, epilepsy with generalised tonic-clonic seizures alone, Dravet syndrome, and progressive myoclonic epilepsies.[7][31][32]
- Seizures may be provoked by external stimuli such as noise.

### developmental delay (common)

- May be present in patients with epilepsy syndromes, and may first become apparent either before or after first seizure occurrence.
- Children with Dravet syndrome have normal development before onset of seizures, but intractable seizures lead to developmental delay, intellectual disability, and sometimes also development of neurological abnormalities such as ataxia.[31]
- Around two-thirds of children with epilepsy with myoclonic-atonic seizures have normal development prior to the onset of epilepsy; developmental delay occurs following onset. Development progresses, but some children will have a degree of intellectual disability.[32]
- Most children with Lennox-Gastaut syndrome have developmental delay, which may be apparent before seizure onset. Over 90% of patients with a diagnosis of Lennox-Gastaut syndrome ultimately have moderate to severe intellectual disability.[32]
- Patients with epilepsy with myoclonic absence may have intellectual impairment at seizure onset, and intellectual disability is ultimately found in around 70% of patients.[32]
- It may be difficult to identify absence seizures or even absence status epilepticus in a child with developmental delay.

### neurocutaneous stigmata (uncommon)

- Conditions with neurocutaneous signs can manifest with seizures.[12]
- Tuberous sclerosis complex: depigmented macules, shagreen patches, periungual fibromas, adenoma sebaceum, and ash-leaf macules.
- Neurofibromatosis type 1: cafe au lait spots, axillary and inguinal freckling, and plexiform neurofibromas.
- Sturge-Weber syndrome: port wine-coloured haemangiomas on the face or trunk.

# Risk factors

## Strong

### genetic predisposition or family history

- Most (but not all) recurrent generalised seizures are due to epilepsy syndromes with a genetic or presumed genetic aetiology.[3]
- Some epilepsies are the result of monogenic inheritance; the genes responsible have been identified for some of the epilepsies in this group, such as familial neonatal seizures.[6]
- However, for many epilepsies the patterns of inheritance are complex. Examples include the idiopathic epilepsies childhood absence epilepsy, juvenile absence epilepsy, and juvenile myoclonic epilepsy.[6]

### antenatal or perinatal insults

- Antenatal and perinatal insults are the most common cause of preventable aetiologies of epilepsy. These include fetal distress or asphyxia, and neonatal infection.[10]

### metabolic/neurodegenerative disorders

- Abnormal metabolic states (e.g., hypoglycaemia, hypocalcaemia) can often provoke seizures.
- Recurrent seizures are part of a clinical picture of many metabolic/neurodegenerative disorders in childhood, although the background of this association is often not fully understood.

### traumatic brain injury

- Moderate or severe traumatic brain injuries may lead to recurrent seizures, which are known as post-traumatic epilepsy; however, focal seizures are more common in this setting.[10]
- Estimates of how many people will develop post-traumatic epilepsy after brain trauma vary depending on the population studied. In one UK study, 9% of children who received inpatient rehabilitation for head injury went on to develop post-traumatic epilepsy.[11] The proportion of epilepsy among children that is attributable to traumatic brain injury is greater in low- and middle-income than in high-income countries.[10]

### structural abnormalities of the central nervous system (CNS)

- Structural lesions of the brain often lead to recurrent seizures; however, they are usually focal rather than generalised seizures, although in some cases there may be rapid bilateral spread leading to generalised seizure. Diffuse structural abnormalities, such as lissencephaly, can be associated with generalised seizures.

### neurocutaneous syndromes

- Conditions with neurocutaneous signs can manifest with seizures. These include tuberous sclerosis complex (depigmented macules, shagreen patches, periungual fibromas, adenoma sebaceum, and ash-leaf macules), neurofibromatosis type 1 (cafe au lait spots, axillary and inguinal freckling, and plexiform neurofibromas), and Sturge-Weber syndrome (port wine-coloured haemangiomas on the face or trunk).[12]

### history of febrile seizures

- Many studies show that a history of febrile seizures increases the risk of epilepsy, and this increased risk persists into adult life.[13]
- Most common seizure types after febrile seizures are generalised tonic-clonic seizures, absence seizures, and focal motor seizures.
- A genetic component has been suggested for febrile seizures.[14] Among children with a history of febrile convulsions, those who had complex febrile seizures, have a family history of epilepsy, or have developmental delay are at most risk of developing epilepsy.[15]

## Weak

### autistic spectrum disorder

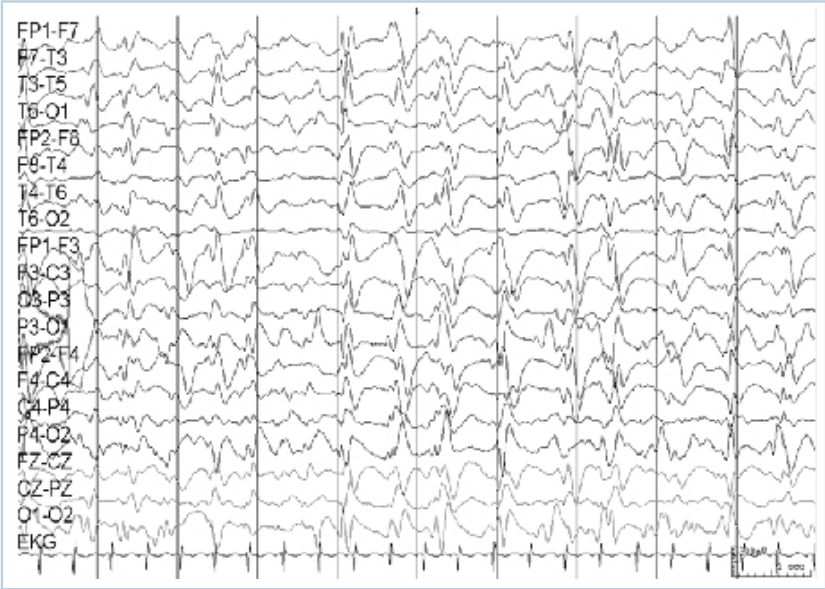
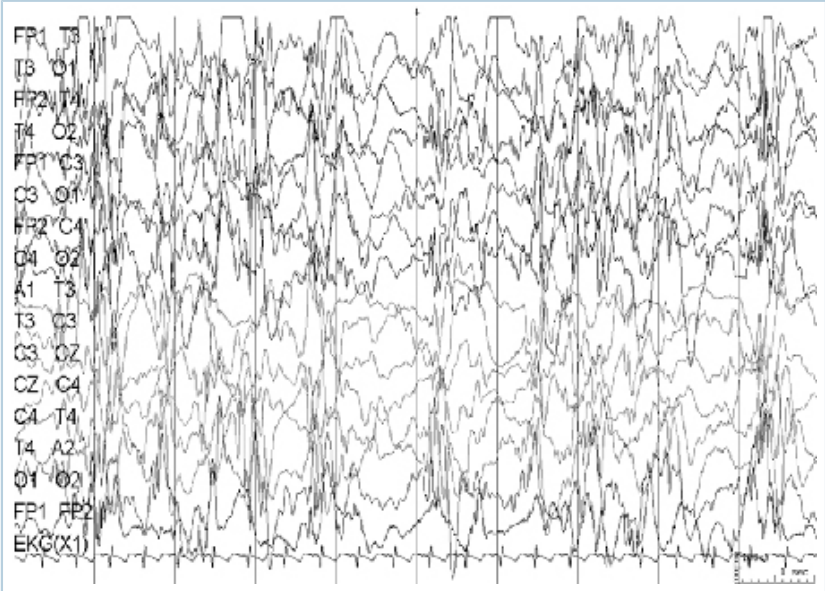
- Approximately 20% to 35% of patients with autistic spectrum disorder have a seizure disorder; however, focal seizures are more common than generalised seizures.[16] [17]
- An increase in epilepsy is seen with increasing age in children with autism spectrum disorder.[16]

### CNS infection

- CNS infections such as meningitis, encephalitis, or parasitic infections may result in recurrent seizures beyond the setting of the acute infection. These are often focal in onset.[10]

# Investigations

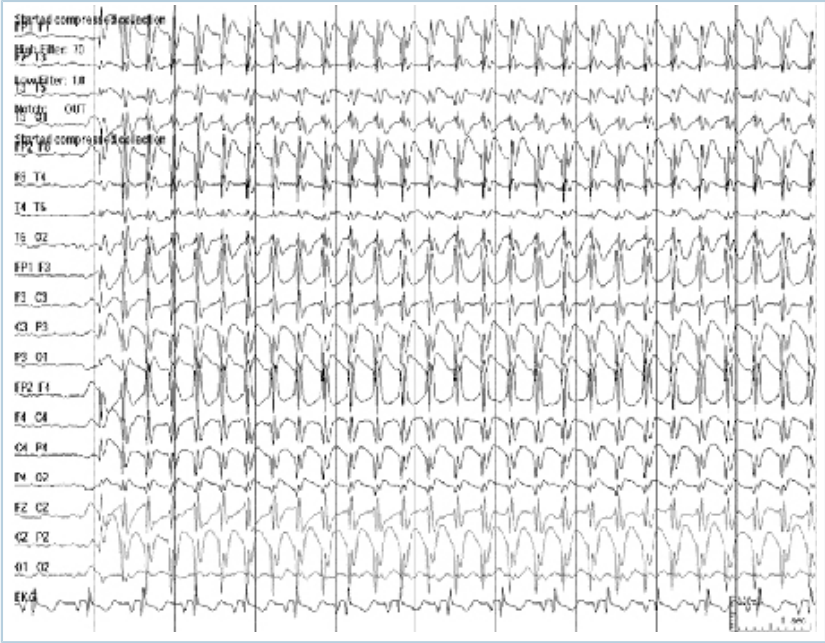
## 1st test to order

| Test | Result |
|---|---|
| **electroencephalogram (EEG)**<br>• Standard diagnostic test.[23]<br>• Epileptic discharges may be seen on the inter-ictal recording. Abnormal rhythms are usually characteristic for specific types of epilepsy syndrome.<br>  <br>*Electroencephalogram (EEG): epilepsy with myoclonic-atonic seizures*<br>*Courtesy of Professor Eric Kossoff; used with permission*<br>  <br>*Electroencephalogram (EEG): Lennox-Gastaut syndrome*<br>*Courtesy of Professor Eric Kossoff; used with permission* | **abnormal rhythms specific to epilepsy syndrome; details for each syndrome are described in Diagnostic approach** |

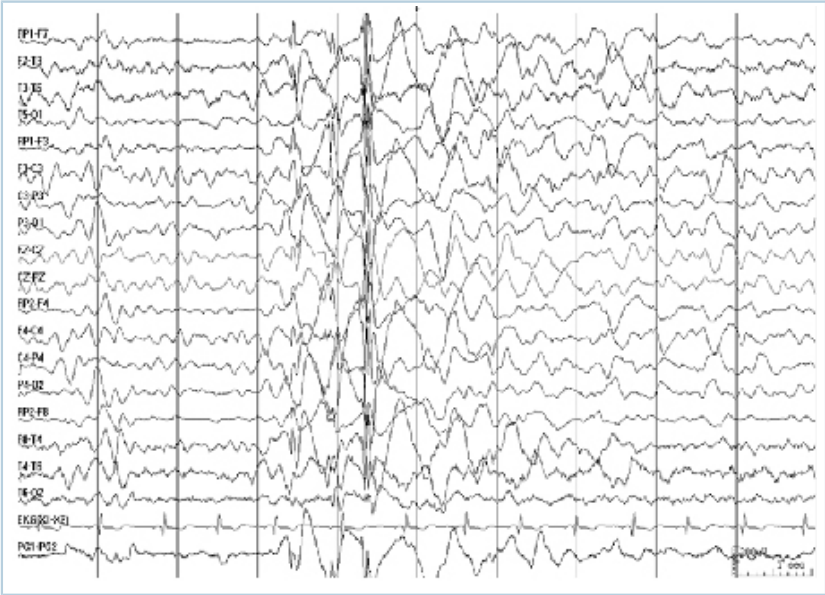


| Test | Result |
| --- | --- |



*Electroencephalogram (EEG): childhood absence epilepsy; shows typical 3 per second spike-and-wave pattern*
*Courtesy of Professor Eric Kossoff; used with permission*



*Electroencephalogram (EEG): juvenile myoclonic epilepsy*
*Courtesy of Professor Eric Kossoff; used with permission*

- Up to 40% of children with epilepsy have normal inter-ictal EEGs; therefore a normal inter-ictal EEG does not exclude a diagnosis of epilepsy.
- Hyperventilation, photic stimulation, and sleep deprivation may be used to provoke seizures.
- A video EEG may be used to determine whether the clinically observed seizures are epileptiform in nature.

| Test | Result |
|---|---|
| **blood glucose level**<br>• Blood glucose measurement is an obligatory part of evaluation for any child with decreased consciousness level.<br>• Should be ordered at least once for all patients with recurrent seizures. | **decreased in the presence of hypoglycaemia** |
| **basic metabolic panel**<br>• Ordered to exclude metabolic disorders or electrolyte imbalances if a secondary cause is suspected.<br>• Should be ordered at least once for all patients with recurrent seizures. | **abnormal in the presence of metabolic or electrolyte abnormalities** |
| **FBC**<br>• Ordered to exclude infection if a secondary cause is suspected.<br>• Should be ordered at least once for all patients with recurrent seizures. | **normal or elevated WBC count** |
| **ECG**<br>• Ordered to exclude cardiac causes of seizure-like episodes. Particular attention should be given to the length of corrected QT interval.[27] [28]<br>• A cardiologist should be consulted if there is doubt or if there is a family history of early unexplained death. | **usually normal** |

## Other tests to consider

| Test | Result |
|---|---|
| **MRI brain**<br>• EEG and clinical picture is usually diagnostic; however, in cases where diagnosis is in doubt or a secondary cause is suspected, MRI is the definitive imaging technique in children, as it does not involve ionising radiation and the images give more detail than CT scans.[29] | **no underlying pathology in idiopathic generalised seizures; may reveal cause in patients with symptomatic epilepsy** |
| **CT brain**<br>• CT has a role in acute investigation for children with a recent history of a seizure and in whom an intracerebral bleed needs to be ruled out. It is also used when there are concerns about a space-occupying lesion and an MRI is not available.[29] | **no underlying pathology in idiopathic generalised seizures; may reveal cause in patients with symptomatic epilepsy** |
| **genetic testing**<br>• Genetic testing is recommended for children with suspected Dravet syndrome. It should also be considered for suspected developmental and epileptic encephalopathies (including suspected early infantile developmental and epileptic encephalopathy, Lennox-Gastaut syndrome, and infantile epileptic spasm syndrome), or if structural abnormalities suggest a genetic cause.[21] [31] [32][33] | **mutations specific to epilepsy syndrome identified** |

# Differentials

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| **Functional seizures (non-epileptic seizures)** | • Episodes of altered movement, sensation, emotion, or experience that have the appearance of epileptic seizures but are not caused by paroxysmal, hypersynchronous electrical activity of the brain.[35]<br>• The clinical appearance of functional seizures may mimic virtually any seizure type.<br>• Some features more likely to suggest functional seizures include: eyes being tightly closed, tearfulness, duration more than 2 minutes, hyperventilation during a seizure, and side-to-side head shaking.[36]<br>• Functional seizures are usually considered a functional neurological symptom disorder. Some patients will have had adverse life events, but, importantly, these are neither necessary nor sufficient for the diagnosis.[36]<br>Psychological comorbidities - especially anxiety, panic, and depression - are common, affecting over 50% of patients.[37]<br>• A significant minority of people with functional seizures will have co-existent epilepsy, so it is important to determine whether the patient has a number of different types of spell. | • The only reliable diagnostic test to differentiate functional from epileptic seizures is video electroencephalogram (EEG) (long-term monitoring). The EEG during functional seizures is either normal or obscured by movement or muscle artefact.<br>• Correct diagnosis is usually based on the semiology of the event and the absence of epileptiform EEG correlate. |
| **Breath-holding spells (prolonged cyanotic expiratory apnoea)** | • Often precipitated by anger or frustration.<br>• Typically vigorous cry is followed by a period of blocked respiration resulting in cyanosis, loss of consciousness, and sometimes opisthotonic posturing (i.e., muscle spasm leading to | • ECG during the event may show initial tachycardia followed by bradycardia. |

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| | pronounced hyper-extension with head and lower limbs bent backwards and the trunk arched forwards). | |
| **Long QT syndrome** | • Often positive family history.<br>• History of syncope triggered by pain, fear, or exercise. | • ECG shows prolonged corrected QT interval.<br>• No epileptic discharges on EEG during the episode but, depending on the duration of asystole, hypoxic slowing of the EEG may be seen during the attack. |
| **Syncope** | • Often happens in standing position and is accompanied by pallor and sweating.<br>• May be precipitated by painful stimuli.<br>• Usually quick recovery and no post-ictal phase. | • Tilt-table testing can confirm a diagnosis of vasovagal syncope, the most common type.<br>• 12-lead ECG is the only test needed and excludes prolonged QT syndrome. |
| **Parasomnias** | • Occur mostly in the first few hours of sleep and usually not repetitive in same night.<br>• Sleep behaviours such as sleepwalking and eating while asleep may be present. | • Normal EEG during the event. |
| **Paroxysmal movement disorders** | • Includes tics, episodic ataxias, or paroxysmal dyskinesias.<br>• Occasionally characteristics of the movements (e.g., location, speed, frequency) are different from seizure. | • Normal EEG during the event. |
| **Gastro-oesophageal reflux** | • Characterised by child gasping and becoming suddenly apnoeic and stiff.<br>• May be a change of skin colour.<br>• Child may appear startled.<br>• Bizarre posturing that may accompany this event is known as Sandifer syndrome.<br>• Usually occurs within 1 hour or so of a feed. | • Trial of treatment with H2 antagonists, proton-pump inhibitors, or antacids terminates the events. |
| **Inattention/daydreaming** | • Episodes can be interrupted and do not finish suddenly.<br>• Not accompanied by automatisms. | • Inter-ictal and ictal EEG are normal. |

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| **Panic disorders** | • Panic attacks usually occur during periods of stress.<br>• May be accompanied by chest pain or paraesthesias.<br>• No post-ictal phase. | • Normal EEG during the event. |
| **Self-gratification behaviour** | • Infantile masturbation may be confused with seizure disorder.<br>• Rhythmic hip flexion and adduction accompanied by a distant expression.<br>• Period of sleepiness afterwards should not be confused with post-ictal phase. | • Normal EEG during the event. |
| **Reflex anoxic seizures** | • Also called reflex asystolic syncope.<br>• Usually precipitated by mild injury.<br>• Cerebral hypoxia may lead to opisthotonic posturing and brief clonic movements.<br>• No post-ictal phase. | • An ECG during the event will document asystole. |
| **Febrile seizures** | • Presence of fever. | • Diagnosis is clinical.<br>• EEG is normal. |

# Approach

Management for the prevention of seizures depends on the epilepsy syndrome, as defined by the International League Against Epilepsy (ILAE).[1][3] [7] [31] [32] Management of the more common epilepsy syndromes with predominantly generalised-onset seizures recognised in childhood will be discussed here. Sometimes the specific epilepsy syndrome cannot be diagnosed, but the patient will still require treatment.

Treatment should be managed initially by a neurologist trained in epilepsy.[27] Epilepsy may worsen the quality of life of a child and family, causing serious hazards including physical injury and sudden death, and influence social aspects of everyday life. Even if epilepsy is successfully treated, some children may still have an impaired quality of life in relation to their own self-esteem, epilepsy comorbidities, and adverse effects associated with therapy.

The main treatment options include anticonvulsant drugs, non-drug therapies such as ketogenic diets and vagus nerve stimulation, and lifestyle measures (i.e., avoiding any precipitating stimuli such as sleep deprivation and alcohol consumption). In children with drug-resistant epilepsies, referral to an epilepsy surgery centre is advised for further evaluation and consideration of treatment options, even in the absence of clear localisation of seizures on video electroencephalogram (EEG) or on structural imaging.[38] [39]

Acute management of status epilepticus (defined as either 5 minutes or more of continuous seizure activity, or two or more discrete seizures between which there is incomplete recovery of consciousness) is beyond the scope of this topic. See Status epilepticus .

## Management of acute repetitive seizures

Acute repetitive seizures (also known as seizure clusters) affect up to half of patients with epilepsy, and can significantly disrupt patients' lives, but their prevalence is under-appreciated and seizure action plans are often lacking.[40] [41]

There is no well-established definition of acute repetitive seizures, which adds to the challenge of recognising them.[42] One frequently used clinical definition is three or more seizures within 24 hours for patients whose habitual seizure frequency is fewer than three seizures per day, with return to full alertness between seizures. Other definitions include two or more seizures in 6 hours, two or more seizures in 24 hours, or two to four seizures in less than 48 hours.[42]

When a convulsive seizure starts in a child, the child should be immediately placed on their side to prevent injury, and the airway cleared. The child's parents and other carers should be trained to administer treatments as soon as possible in the community when seizure clusters are identified, without the need for the patient to attend the hospital.

Treatment options include rectal or intranasal diazepam, or buccal or intranasal midazolam. These benzodiazepine formulations have shown reasonable efficacy, equal to or better than that of intravenous formulations, in most patients. Oral benzodiazepines (e.g., lorazepam) can be used if the above formulations are not available, provided that the patient is awake and cooperative, and the risk of aspiration is low or not a concern.[40] [41]

In a hospital setting, parenteral benzodiazepines (e.g., diazepam, lorazepam) or intravenous formulations of anticonvulsants such as phenytoin (or fosphenytoin), valproate, levetiracetam, lacosamide, phenobarbital, and brivaracetam can be used to treat acute repetitive seizures.

The patient should be continued on a suitable oral formulation of an anticonvulsant once stabilised.

## Anticonvulsant drugs: principles of treatment

Anticonvulsants are the first-line treatment for most epilepsy syndromes and are used long term for prevention of seizures. Long-term therapy is indicated only when attacks are of a true epileptic nature and not a manifestation of another treatable disease process. Incorrect diagnosis leads to inadequate and potentially harmful treatment.

The main goal of treatment is to prevent further seizures. Where possible, diagnosis of a specific epilepsy syndrome or underlying cause aids choice of anticonvulsant and guides length of treatment. Drug treatment is usually started after the second unprovoked seizure.[43]

Choice of anticonvulsant is an important decision. Choice should be individualised, taking into account efficacy in a specific syndrome and potential adverse effects. Studies have shown that only a few drugs can control idiopathic generalised epilepsies without potentially causing seizure aggravation.[44]

Monotherapy is preferred, as it decreases the risk of adverse effects and drug interactions, and allows the physician to find the right balance between symptom control and toxicity.[45] However, some of the described syndromes often fail to respond to monotherapy, and combination therapy is required. In these situations, it is important to take into account any interactions between the chosen anticonvulsants, as well as any interactions with other drugs the patient may be taking. The dose of certain anticonvulsants needs to be adjusted according to serum drug levels.

Anticonvulsant drugs may be associated with a small increased risk of suicidal thoughts and behaviour. People with epilepsy are also at higher risk of mood and anxiety disorders and suicidal ideation at the time of diagnosis, before starting anticonvulsant medications, and risk of suicide associated with these medications is much lower than the risk of harm due to stopping medications or not starting them.[46] [47]

## Considerations for patients of child-bearing potential

Patients with the potential to become pregnant should be provided with information from early adolescence about the risk of unplanned pregnancy, contraceptive options, and potential adverse pregnancy outcomes. Anticonvulsants with enzyme-inducing properties can lower contraceptive efficacy and lead to an increased failure rate.[48]

For patients of child-bearing potential, the safety of anticonvulsants in pregnancy must be taken into account in choice of medication.

Valproate and its analogues

In both the US and Europe, valproate and its analogues are contraindicated during pregnancy due to the risk of congenital malformations and developmental problems in the child. If it is not possible to stop valproate, treatment may be continued with appropriate specialist care. Valproate and its analogues must not be used in patients of child-bearing potential unless there is a pregnancy prevention programme in place and certain conditions are met.[49] If the patient is taking the drug to prevent major seizures and is planning to become pregnant, the decision of continuing valproate versus changing to an alternate agent should be made on an individual basis.

Safety of other anticonvulsants

A review of the safety of anticonvulsants (other than valproate) in pregnancy by the UK Medicines and Healthcare products Regulatory Agency (MHRA) concluded that lamotrigine and levetiracetam, at maintenance doses, are not associated with an increased risk of major congenital malformations. Available studies also do not suggest an increased risk of neurodevelopmental disorders or delay associated with in-utero exposure to lamotrigine or levetiracetam, but data are more limited.[50] A later study suggested an association between antenatal exposure to levetiracetam and ADHD.[51]

Data for other drugs show an increased risk of major congenital malformations associated with carbamazepine, phenobarbital, phenytoin, and topiramate; possible adverse effects on neurodevelopment of children exposed in utero to phenobarbital and phenytoin; and an increased risk of fetal growth restriction associated with phenobarbital, topiramate, and zonisamide. Risks associated with other anticonvulsants are uncertain due to limitations in the data.[50] [52] [53] One subsequent MHRA study suggested that pregabalin might slightly increase the risk of major congenital malformations.[54] One large cohort study reported an association between antenatal exposure to topiramate and increased risk of child neurodevelopmental disorders; the use of topiramate in patients of child-bearing potential is being reviewed by the European Medicines Agency (EMA) and the MHRA.[55] [56] [57] One systematic review reported adverse fetal and neonatal outcomes following in-utero exposure to oxcarbazepine.[52]

## Non-pharmacological treatment options

Non-pharmacological treatment options may need to be explored, especially for refractory epilepsy.[39] [58] [59] [60] [61] Referral to an epilepsy surgery centre is advised for further evaluation and consideration of treatment options.[38] [39] Surgery is only rarely recommended for patients with generalised-onset seizures.

Ketogenic diets

Ketogenic diets are high in fat and low in carbohydrates, and have been demonstrated to be effective in reducing seizure frequency in children with drug-resistant epilepsy. A ketogenic diet should be considered after two anticonvulsant drugs have proved ineffective, and even earlier for several epilepsy syndromes. There are four main types of ketogenic diet (the 'classic' ketogenic diet, the modified Atkins diet, the medium chain triglyceride diet, and the low glycaemic index treatment), and choice should be individualised, taking into account the situation of the family and child and the expertise of the clinical team. Use of a ketogenic diet requires a skilled team, including a dietitian. The classic ketogenic diet is usually started in hospital, under close medical supervision, and regular monitoring is required.[39] [60] [61]

Vagus nerve stimulation

Vagus nerve stimulation is an effective and safe adjunctive therapy in patients with medically refractory epilepsy not amenable to resection. However, some patients do not receive any benefit from this therapy. Common adverse effects include local skin irritation, headache, nasopharyngitis, and voice alteration. Children should be carefully monitored for site infection.[62] [63] [64] [65]

## Management of epilepsy syndromes with onset in infancy (1 month to 2 years)

Early infantile developmental and epileptic encephalopathy (EIDEE):

- This condition is a severe, very difficult to treat epileptic encephalopathy with potential metabolic, genetic, and structural aetiologies.



- Recognition of metabolic causes of EIDEE is essential to initiate appropriate treatment, if available, and prevent long-term sequelae. However, treatment should not be withheld while waiting for test results.
- Pyridoxine-dependent epilepsy is an important and potentially treatable cause of early-onset therapy-resistant epilepsy. Prompt recognition is important for treatment and prognosis. Infants with early-onset therapy-resistant epilepsy should receive pyridoxine with or without additional anticonvulsants until pyridoxine-dependent epilepsy is fully excluded by metabolic and/or genetic analysis.[66]
- Conventional anticonvulsants are options for treatment of EIDEE, but their efficacy is limited. Zonisamide, vigabatrin, topiramate, and high doses of phenobarbital may be of some value.[67] [68] [69]
- Sodium-channel-blocking drugs, such as oxcarbazepine, should be considered optimal therapy when the epileptic encephalopathy is suspected to be due to gain-of-function pathogenic variants of SCN2A/SCN8A or loss-of-function KCNQ2 variants.
- Quinidine has been used to treat epilepsy associated with gain-of-function KCNT1 variants, but studies have yielded contradictory results.[70] [71]
- Ketogenic diets should be considered for patients with refractory epilepsy.[60] [61]
- Surgery (resection, disconnection) may be effective if the majority of seizures are focal and due to an identified structural cause. It is important to identify potential structural aetiology and consider surgery early if seizures are refractory to drug treatment.[72]

Infantile epileptic spasms syndrome (IESS; including West syndrome):

- Epileptic spasms are resistant to most anticonvulsants. An oral corticosteroid, corticotropin (ACTH), or vigabatrin (the treatment of choice for patients with tuberous sclerosis complex) should be used as initial treatment as soon as infantile epileptic spasms are diagnosed, as all have shown efficacy in studies.[73] [74] [75] [76]
- ACTH and corticosteroids have similar reported efficacy for IESS: 46% and 44% of patients, respectively, showed a response to treatment in one study. Response rates to vigabatrin were 62% for infants with tuberous sclerosis complex and 29% for those with other causes of infantile spasms.[77] The presence or absence of hypsarrhythmia should not impact treatment decisions.[78]
- Recommendations regarding drug regimen, doses, and duration of treatment vary. The most common regimen is ACTH, followed by a corticosteroid (usually prednisolone). Treatment dose may need to be escalated quickly in an attempt to stop spasms and improve EEG.
- If the first treatment is ineffective, an alternative medication from the initial options with a different mechanism of action should be tried, as these are more effective than using standard anticonvulsants: that is, vigabatrin if prednisolone or ACTH was used as the primary option, and prednisolone or ACTH if vigabatrin was used as the primary option.[79]
- Alternatively, prednisolone or ACTH may be used in combination with vigabatrin: there is some evidence for improved seizure control with combination therapy, but no good evidence that it changes long-term outcomes.[80]
- There is insufficient evidence for efficacy of other anticonvulsants for the treatment of refractory infantile spasms. Medication choices should be made on an individual patient-specific basis. Medications used have included topiramate, clobazam, valproate, zonisamide, levetiracetam, and phenobarbital. Valproate is contraindicated in patients with urea cycle disorders and some mitochondrial disorders, especially those caused by mitochondrial DNA polymerase gamma, and should be avoided in children under age 2 years unless these causes are excluded.[79] [81]

- Pyridoxine is sometimes used as a treatment option, although one study reported that add-on pyridoxine was ineffective.[82] [83] [84]
- Ketogenic diets are an effective option for intractable epileptic spasms.[61] However, effects may be temporary, so use of a ketogenic diet is reserved for hormone-resistant cases.
- For children with drug-resistant epileptic spasms who have localised brain abnormalities (especially when they correlate with EEG localisation), surgery (resection, disconnection) is considered appropriate. Structural abnormalities (e.g., tumours, porencephaly, hemimegalencephaly) are indications for surgery with good potential outcome. Focal cortical dysplasia is also an indication for surgery, especially if it correlates with EEG findings. Early surgery is suggested for drug-resistant cases, because early intervention may lead to better cognitive prognosis.

Myoclonic epilepsy in infancy (MEI):

- Seizure control is usually favourable, with patients who show a quick response appearing to have a better outcome.
- Valproate monotherapy is generally considered effective in patients with MEI.[85] [86] Valproate is contraindicated in patients with urea cycle disorders and some mitochondrial disorders, especially those caused by mitochondrial DNA polymerase gamma, and should be avoided in children under age 2 years unless these causes are excluded.
- Other treatment options include topiramate, lamotrigine, clonazepam, and levetiracetam.[67]
- There is a suggestion that delays in the start of treatment may cause cognitive problems later in life.[87]
- Some patients originally diagnosed with MEI may develop other types of epilepsy, particularly juvenile myoclonic epilepsy.[31]

Dravet syndrome:

- Valproate and clobazam are recommended as initial therapies.[21] [88] [89]
- If valproate and clobazam are insufficiently effective, stiripentol and/or fenfluramine should be considered.[21] [88] [89]
- Stiripentol (a cytochrome P450 inhibitor that increases blood levels of other anticonvulsants) is effective when added to clobazam, and when used as monotherapy (off-label). It is approved as adjunctive therapy (with clobazam) for Dravet syndrome in children from age 6 months.[21] [89] [90]
- Fenfluramine (a serotonin receptor agonist) is approved to treat seizures related to Dravet syndrome in patients aged 2 years and older. It may be used as monotherapy or in combination with other drugs. In randomised controlled trials, fenfluramine resulted in significantly greater reduction in the frequency of convulsive seizures compared with placebo.[21] [91] [92]
- Cannabidiol oral solution is approved for the treatment of seizures associated with Dravet syndrome for patients aged 1 year and older (2 years and older in some other countries). Pharmaceutical-grade cannabidiol is associated with a decrease in the frequency of seizures related to Dravet syndrome, although the mechanism of action is unknown.[93] [94] [95] There is evidence that cannabidiol is effective in the absence as well as in the presence of clobazam.[96] [97]
- Sodium-channel-blocking drugs such as carbamazepine, oxcarbazepine, lamotrigine, and phenytoin are known to exacerbate seizures in children with Dravet syndrome, and should be avoided.[21] [89]
- Topiramate may be used as monotherapy or adjunctively. Efficacy of topiramate when used as adjunctive therapy for Dravet syndrome has been reported.[21] [98]
- Ketogenic diets are effective, and should be considered after two unsuccessful anticonvulsant trials, or earlier in some cases.[21] [61]

- Vagus nerve stimulation typically results in a <50% reduction in seizures, but should be considered only after other therapeutic options have been tried.[21]

Genetic epilepsy with febrile seizures plus (GEFS+), which includes febrile seizures plus (FS+)

- Seizures typically respond to treatment with anticonvulsants.[31] Treatment options include valproate, lamotrigine, levetiracetam, or topiramate.

## Management of epilepsy syndromes with onset in childhood

Childhood is defined as ages 2-12 years.[32]

Epilepsy with myoclonic-atonic seizures (EMAtS; also known as Doose syndrome):

- Approximately one third of children show a response to anticonvulsants, and less than 10% are seizure-free after anticonvulsant treatment.[99] Valproate is recommended most often as first-line therapy.[100] [101]
- Ketogenic diets are highly effective for this syndrome.[61] [99] [101] In one study of a large retrospective multi-centre cohort, therapy with a ketogenic diet was by far the most effective treatment, and it therefore should be considered as initial therapy.[99]
- Options for second-line treatment with evidence of effectiveness are benzodiazepines (e.g., clobazam, clonazepam), levetiracetam, zonisamide, and topiramate.[101]
- Lamotrigine, ethosuximide, rufinamide, perampanel, and felbamate also have some evidence of effectiveness.[101]
- Vigabatrin and sodium-channel-blocking drugs other than lamotrigine should be avoided.[101]
- Vagus nerve stimulation or corpus callosotomy (for drop attacks) may be considered only if medications and ketogenic diets are insufficiently effective.[101]

Lennox-Gastaut syndrome (LGS):

- LGS is significantly resistant to therapy, and monotherapy with an anticonvulsant is rarely effective. This often means that polytherapy at high doses is required, which may lead to a paradoxical increase in seizure frequency.
- Careful discussion with carers about treatment goals is necessary to balance seizure control with medication adverse effects. Goals are typically to decrease the burden of seizures that are prolonged or associated with injury, but seizure freedom is unlikely.
- Valproate is the most commonly used first-line agent. Clobazam may also be considered first line as monotherapy, or in combination with valproate.
- Other anticonvulsants with evidence of effectiveness for treating seizures associated with LGS include rufinamide, lamotrigine, topiramate, cannabidiol, and fenfluramine.[102] [103] [104] [105] [106]
- Cannabidiol oral solution is approved for the treatment of seizures associated with LGS for patients aged 1 year and older (2 years and older in some other countries). In randomised, double-blind, placebo-controlled trials, adjunctive cannabidiol oral solution effectively reduced the frequency of drop seizures compared with placebo.[104] [107] [108][109] There is some evidence that cannabidiol is effective in the absence as well as in the presence of clobazam.[96] [97] Adverse effects of cannabidiol include elevated liver enzymes, gastrointestinal intolerance, and sleep disturbances.[94][110]
- Fenfluramine is approved for the treatment of seizures associated with LGS in patients aged 2 years and older. One randomised controlled trial and an open-label extension study showed that fenfluramine resulted in a significantly greater reduction in drop seizures than placebo in patients

with LGS; this effect appeared to be greatest in patients with generalised tonic-clonic seizures.[111] [112]

- Other anticonvulsants that may be considered include levetiracetam, perampanel, zonisamide, felbamate, lacosamide, brivaracetam, and cenobamate (not licensed for use in children), although in some cases evidence of effectiveness in LGS is scarce or uncertain.[102] [104] [105] [113]
- Carbamazepine, eslicarbazepine, gabapentin, oxcarbazepine, phenytoin, pregabalin, and vigabatrin may exacerbate seizures associated with LGS, and so are usually avoided.[105]
- Corticosteroids and/or corticotropin (ACTH) may be indicated for short-term adjunctive treatment during a particularly difficult period (i.e., at onset, in status epilepticus, or during a period of significant seizure exacerbation).
- Non-pharmacological therapies that may be tried include ketogenic diets, vagus nerve stimulation, corpus callosotomy, or (if there is a dominant and/or structural seizure focus) resective surgery.[61] [104] [114]

Childhood absence epilepsy (CAE):

- Generalised-onset tonic-clonic seizures occur in some absence epilepsies. In this case, treatment should be directed at treating both the tonic-clonic seizures and the absences.[7]
- In children with absence seizures only, ethosuximide is the first-line option.[115] Valproate is the recommended first-line anticonvulsant for patients with both absences and tonic-clonic seizures, but the adverse-effect profile is not as favourable as that of ethosuximide.[115] [116] [117]
- One Cochrane review supports the use of lamotrigine and levetiracetam as suitable alternatives to valproate, particularly for patients of child-bearing potential for whom valproate may not be an appropriate therapy due to teratogenicity.[116] Lamotrigine may be added to valproate therapy, or other polypharmacy may be required, for refractory cases.[27][118]
- Topiramate, benzodiazepines, perampanel, and zonisamide are further options.[119] [120] [121]
- Gabapentin is not effective in these patients, and evidence suggests that carbamazepine and vigabatrin may exacerbate absence seizures.[122] Therefore, use of these agents is not recommended.[27]

Epilepsy with myoclonic absence (EMA):

- EMA is often refractory to anticonvulsants, and polypharmacy may be required.
- Anticonvulsants commonly used include valproate, ethosuximide, lamotrigine, levetiracetam, and benzodiazepines.[116] [123]

Epilepsy with eyelid myoclonia (EEM):

- This syndrome tends to be resistant to drug therapy, with up to 80% of patients developing medically intractable epilepsy and requiring polypharmacy. Generalised tonic-clonic seizures are often responsive to treatment, while eyelid myoclonia are not fully controlled.[32] [124]
- Valproate, lamotrigine, and levetiracetam are recommended as first-line treatment options, and may reduce seizures by more than 50%.[124] [125] [126] Levetiracetam and lamotrigine should particularly be considered for patients of child-bearing potential due to the teratogenic risks of valproate.[124] [125]
- There is some evidence for effectiveness of ethosuximide and clobazam.[124] [125]
- Other anticonvulsants (e.g., topiramate, brivaracetam, zonisamide, cannabidiol, fenfluramine, clonazepam, perampanel, lacosamide, and acetazolamide) may be tried, but there is little evidence for effectiveness in EEM and no consensus about their use.[124] [125]
- Cannabidiol can also worsen seizures, especially eyelid myoclonia, and should be used with caution.[125]

- Sodium-channel-blocking drugs, except for lamotrigine, may worsen seizures and should be avoided.[124] [125]
- Data on the use of ketogenic diets in EEM are limited.[124] [125]
- Lens therapy may be trialled for patients with a photoparoxysmal response, although evidence for effectiveness is limited.[124] [125]

## Management of epilepsy syndromes with onset at a variable age

Onset of these syndromes often occurs in late childhood/adolescence (from 10 years of age).[7]

See also 'Considerations for patients of child-bearing potential'.

Epilepsy with generalised tonic-clonic seizures alone (GTCA):

- Lifestyle measures may need to be implemented to achieve freedom from seizures. Patients should be warned of common seizure precipitants including sleep deprivation and alcohol consumption.[127]
- First-line treatment is valproate.[116]
- One Cochrane review supports the use of lamotrigine and levetiracetam as suitable alternatives to valproate, particularly for patients of child-bearing potential for whom valproate may not be an appropriate therapy due to teratogenicity.[116] Lamotrigine is also effective as an adjunctive therapy in controlling primary generalised tonic-clonic seizures.[128]
- Clobazam and topiramate (monotherapy or with valproate) are also effective options.[129] [130] [131]
- Perampanel is well tolerated and improves control of drug-resistant primary generalised tonic-clonic seizures in idiopathic generalised epilepsy when used adjunctively in patients aged 12 years or older.[120] [132]
- Carbamazepine may aggravate seizures in patients with idiopathic generalised epilepsies and so is not recommended.[27]
- Vagus nerve stimulation and ketogenic diets are treatment options for patients with drug-resistant idiopathic generalised epilepsy.[59][61] [133]

Juvenile myoclonic epilepsy (JME):

- Lifestyle adjustments (avoiding sleep deprivation and alcohol consumption) and lifelong anticonvulsant therapy are required in these patients.[127]
- First-line option is valproate. It may be used alone, or in combination with lamotrigine in resistant cases.[116][134]
- One Cochrane review supports the use of lamotrigine and levetiracetam as suitable alternatives to valproate, particularly for patients of child-bearing potential for whom valproate may not be an appropriate therapy due to teratogenicity.[116]
- Levetiracetam is considered the most safe and efficacious of the newer anticonvulsants when used as monotherapy.[135] [136] [137]
- Monotherapy with lamotrigine is controversial as, despite its efficacy in controlling tonic-clonic seizures and absences, there is a very high risk of aggravation of myoclonic jerks.[138]
- Additional treatment options include topiramate, zonisamide, and perampanel.[120] [139] [140]
- Carbamazepine may aggravate seizures in patients with idiopathic generalised epilepsies and so is not recommended.[27]

Juvenile absence epilepsy (JAE):

- JAE is more likely to result in tonic-clonic seizures and is less likely to be outgrown than childhood absence epilepsy.
- Lifestyle adjustments (avoiding sleep deprivation and alcohol consumption) and lifelong anticonvulsant therapy are required in these patients.[127]
- First-line anticonvulsant is ethosuximide for patients with absence seizures only. If seizures persist with ethosuximide or if there are generalised tonic-clonic seizures, valproate is preferred.[116] [141]
- One Cochrane review supports the use of lamotrigine and levetiracetam as suitable alternatives to valproate, particularly for patients of child-bearing potential for whom valproate may not be an appropriate therapy due to teratogenicity.[116]
- Additional treatment options include clobazam, topiramate, zonisamide, and perampanel.[120] [141] [142]

## Unidentified epilepsy syndrome

Sometimes an epileptic syndrome cannot be diagnosed. Anticonvulsant therapy must be tailored to the individual patient and is based on seizure types, age, sex, and comorbidities. Monotherapy is preferable, although polypharmacy may be required for seizure control if monotherapy is insufficiently effective. A careful balance of seizure control and anticonvulsant adverse effects should be maintained.

If seizures are generalised in onset, or it is not known whether onset is focal or generalised, broad-spectrum anticonvulsants are recommended. First-line options include valproate, lamotrigine, levetiracetam, and topiramate.

Valproate is better tolerated than topiramate and more efficacious than lamotrigine, and remains the drug of choice for many patients with generalised and unclassified epilepsies.[143]

Lamotrigine is also effective as an adjunctive therapy in combination with other anticonvulsants in controlling primary generalised tonic-clonic seizures.[128] [134]

Topiramate is well tolerated and effective for prolonged tonic-clonic seizures when used adjunctively with another anticonvulsant or for resistant tonic-clonic seizures when used as monotherapy.[144] [145]

Carbamazepine is indicated for generalised tonic-clonic seizures, but can aggravate absence, myoclonic, and tonic/atonic seizures.[146]

Perampanel is well tolerated and improves control of drug-resistant primary generalised tonic-clonic seizures in idiopathic generalised epilepsy when used adjunctively in patients aged 12 years or older. [120] [142]

## Drug discontinuation

Seizure freedom for long periods of time can occur with anticonvulsant therapy or after surgical treatment. Patients taking anticonvulsants who achieve seizure freedom may eventually wish to discontinue medication to avoid the adverse effects, psychological implications, and cost of ongoing treatment.

For children who have been seizure-free for at least 18-24 months, and who do not have an electroclinical syndrome suggesting otherwise, discontinuation of anticonvulsant medication may be considered, as this does not clearly increase risk of seizure recurrence. The risks and benefits of discontinuation should be discussed with the patient and family, and the known natural history of the specific electroclinical syndrome should be taken into account. Provided that an EEG does not show epileptiform activity, discontinuation should be offered at a rate no faster than 25% every 10-14 days.[147]

Syndromes known to have a high risk of relapse are those with a proven/probable lesional origin (Lennox-Gastaut syndrome, severe myoclonic epilepsy, juvenile myoclonic epilepsy, and awakening generalised tonic-clonic seizures). In these cases, prolonged therapy for up to 5 years, or even lifelong therapy, may be required.

There is little evidence to guide the rate of withdrawal of anticonvulsants.[148]

# Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

| Acute ( summary ) | | |
|---|---|---|
| **acute repetitive seizures (children >1 month of age)** | | |
| **in the community** | **1st** | **benzodiazepine** |
| **in hospital** | **1st** | **parenteral benzodiazepine or anticonvulsant** |

## Ongoing ( summary )

| | | |
|---|---|---|
| **epilepsy syndromes with onset in infancy (1 month to 2 years)** | | |
| ■ **early infantile developmental and epileptic encephalopathy (EIDEE)** | **1st** | **pyridoxine and/or anticonvulsants** |
| | **2nd** | **ketogenic diet or surgery** |
| ■ **infantile epileptic spasms syndrome (IESS) (including West syndrome)** | **1st** | **corticosteroid or corticotropin (ACTH) or vigabatrin** |
| | **2nd** | **alternative anticonvulsants or ketogenic diet or surgery** |
| ■ **myoclonic epilepsy in infancy (MEI)** | **1st** | **anticonvulsants** |
| ■ **Dravet syndrome** | **1st** | **anticonvulsants** |
| | **2nd** | **topiramate** |
| | **2nd** | **ketogenic diet** |
| | **3rd** | **vagus nerve stimulation** |
| ■ **genetic epilepsy with febrile seizures plus (GEFS+)** | **1st** | **anticonvulsants** |
| **epilepsy syndromes with onset in childhood (2-12 years)** | | |
| ■ **epilepsy with myoclonic-atonic seizures (EMAtS; Doose syndrome)** | **1st** | **anticonvulsant and/or ketogenic diet** |
| | **2nd** | **alternative anticonvulsants** |
| | **3rd** | **vagus nerve stimulation or corpus callosotomy** |
| ■ **Lennox-Gastaut syndrome (LGS)** | **1st** | **anticonvulsants** |
| | **adjunct** | **corticotropin (ACTH) and/or corticosteroid** |
| | **2nd** | **non-pharmacological therapies** |
| ■ **childhood absence epilepsy (CAE)** | **1st** | **anticonvulsants** |
| ■ **epilepsy with myoclonic absence (EMA)** | **1st** | **anticonvulsants** |

| Ongoing | | ( summary ) |
|---|---|---|
| ■ epilepsy with eyelid myoclonia (EEM) | 1st | anticonvulsants |
| | adjunct | lens therapy |
| | 2nd | alternative anticonvulsants and/or ketogenic diet |
| | adjunct | lens therapy |
| **epilepsy syndromes with onset at a variable age** | | |
| ■ epilepsy with generalised tonic-clonic seizures alone (GTCA) | 1st | anticonvulsants |
| | adjunct | lifestyle modifications |
| | 2nd | vagus nerve stimulation or ketogenic diet |
| | adjunct | lifestyle modifications |
| ■ juvenile myoclonic epilepsy (JME) | 1st | anticonvulsants |
| | adjunct | lifestyle modifications |
| ■ juvenile absence epilepsy (JAE) | 1st | anticonvulsants |
| | adjunct | lifestyle modifications |
| **unidentified epilepsy syndrome** | | |
| | 1st | anticonvulsants |

# Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

## Acute

**acute repetitive seizures (children >1 month of age)**

**in the community** — **1st** — **benzodiazepine**

### Primary options

» diazepam rectal: children 2-5 years of age: 0.5 mg/kg rectally as a single dose; children 6-11 years of age: 0.3 mg/kg rectally as a single dose; children ≥12 years of age: 0.2 mg/kg rectally as a single dose
May repeat dose in 4-12 hours. Maximum 1 treatment every 5 days or up to 5 treatments per month.

**OR**

» diazepam nasal: children 6-11 years of age and body weight 10-18 kg: 5 mg intranasally as a single dose; children 6-11 years of age and body weight 19-37 kg: 10 mg intranasally as a single dose; children 6-11 years of age and body weight 38-55 kg: 15 mg intranasally as a single dose; children 6-11 years of age and body weight 56-74 kg: 20 mg intranasally as a single dose; children ≥12 years of age and body weight 14-27 kg: 5 mg intranasally as a single dose; children ≥12 years of age and body weight 28-50 kg: 10 mg intranasally as a single dose; children ≥12 years of age and body weight 51-75 kg: 15 mg intranasally as a single dose; children ≥12 years of age and body weight ≥76 kg: 20 mg intranasally as a single dose
May repeat dose after at least 4 hours. Maximum 2 doses per single episode and 1 episode every 5 days or up to 5 episodes per month.

**OR**

» midazolam nasal: children ≥12 years of age: 5 mg (1 spray) intranasally as a single dose
May repeat dose once in opposite nostril after 10 minutes. Maximum 2 doses per

## Acute

single episode and 1 episode every 3 days or up to 5 episodes per month. This dose is for the proprietary intranasal formulation. The injectable formulation may be used intranasally in some locations; consult your local protocol for dose.

**OR**

» midazolam: children ≥1 month of age: 0.2 mg/kg buccally as a single dose, maximum 10 mg/dose
Buccal formulations are available in some countries. In others, the injectable formulation may be used buccally. Consult your local protocols.

### Secondary options

» lorazepam: consult specialist for guidance on dose

» There is no well-established definition of acute repetitive seizures, which adds to the challenge of recognising them.[42] One frequently used clinical definition is three or more seizures within 24 hours for patients whose habitual seizure frequency is fewer than three seizures per day, with return to full alertness between seizures. Other definitions include two or more seizures in 6 hours, two or more seizures in 24 hours, or two to four seizures in less than 48 hours.[42]

» A child having a convulsive seizure should be immediately placed on their side to prevent injury, and the airway cleared. The child's parents and other carers should be trained to administer treatments as soon as possible in the community when seizure clusters are identified, without the need for the patient to attend the hospital.

» Treatment options include rectal or intranasal diazepam, or buccal or intranasal midazolam. These benzodiazepine formulations have shown reasonable efficacy, equal to or better than that of intravenous formulations, in most patients. Oral benzodiazepines (e.g., lorazepam) can be used if the above formulations are not available, provided that the patient is awake and cooperative, and the risk of aspiration is low or not a concern.[40] [41]

## Acute

» The patient should be continued on a suitable oral formulation of an anticonvulsant once stabilised.

**in hospital** **1st** **parenteral benzodiazepine or anticonvulsant**

### Primary options

» diazepam: children ≥1 month of age: 0.15 to 0.2 mg/kg intravenously as a single dose, may repeat dose within 15 minutes, maximum 10 mg/dose

**OR**

» lorazepam: 0.05 to 0.1 mg/kg intravenously as a single dose, may repeat 0.05 mg/kg after 10-15 minutes according to response, maximum 4 mg/dose

### Secondary options

» phenytoin: 15-20 mg/kg intravenously as a loading dose, followed by an additional dose of 5-10 mg/kg after 10-20 minutes according to response, maximum 1500 mg/day

**OR**

» fosphenytoin: 15-20 mg (phenytoin equivalents)/kg intravenously as a loading dose, followed by an additional dose of 5-10 mg (phenytoin equivalents)/kg after 10-20 minutes according to response, maximum 1500 mg (phenytoin equivalents)/day
Fosphenytoin dose expressed as phenytoin equivalents.

**OR**

» phenobarbital: 15-20 mg/kg intravenously as a single dose, followed by 5-10 mg/kg every 15-30 minutes according to response, maximum 1000 mg/loading dose and 40 mg/kg/total dose

**OR**

» sodium valproate: 40 mg/kg intravenously as a single dose, maximum 3000 mg/dose

**OR**

» levetiracetam: 60 mg/kg intravenously as a single dose, maximum 4500 mg/dose

## Acute

**OR**

» lacosamide: consult specialist for guidance on dose

**OR**

» brivaracetam: consult specialist for guidance on dose

» There is no well-established definition of acute repetitive seizures, which adds to the challenge of recognising them.[42] One frequently used clinical definition is three or more seizures within 24 hours for patients whose habitual seizure frequency is fewer than three seizures per day, with return to full alertness between seizures. Other definitions include two or more seizures in 6 hours, two or more seizures in 24 hours, or two to four seizures in less than 48 hours.[42]

» The child should be immediately placed on their side to prevent injury, and the airway cleared.

» In a hospital setting, intravenous benzodiazepines (e.g., diazepam, lorazepam), or intravenous formulations of anticonvulsants such as phenytoin (or fosphenytoin), valproate, phenobarbital, levetiracetam, lacosamide, and brivaracetam can be used to treat acute repetitive seizures. The patient should be continued on a suitable oral formulation of an anticonvulsant once stabilised.

» Valproate is contraindicated in patients with urea cycle disorders and some mitochondrial disorders, especially those caused by mitochondrial DNA polymerase gamma, and should be avoided in children under age 2 years unless these causes are excluded.[79] [81] Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

## Ongoing

**epilepsy syndromes with onset in infancy (1 month to 2 years)**

**early infantile developmental and epileptic encephalopathy (EIDEE)**

**1st** **pyridoxine and/or anticonvulsants**

### Primary options

» pyridoxine: consult specialist for guidance on dose

**OR**

» zonisamide: consult specialist for guidance on dose

**OR**

» vigabatrin: consult specialist for guidance on dose

**OR**

» topiramate: consult specialist for guidance on dose

**OR**

» phenobarbital: consult specialist for guidance on dose

**OR**

» oxcarbazepine: consult specialist for guidance on dose

### Secondary options

» quinidine sulfate: consult specialist for guidance on dose

» Careful efforts to identify genetic, metabolic, and/or structural aetiology are necessary to guide aetiology-specific treatments.

» Pyridoxine-dependent epilepsy is an important and potentially treatable cause of early-onset therapy-resistant epilepsy. Prompt recognition is important for treatment and prognosis. Infants with early-onset therapy-resistant epilepsy of unknown cause should receive pyridoxine with or without additional anticonvulsants until pyridoxine-dependent epilepsy is fully excluded by metabolic and/or genetic analysis.[66]



## Ongoing

» Conventional anticonvulsants are options for treatment of EIDEE, but their efficacy is limited. Zonisamide, vigabatrin, topiramate, and high doses of phenobarbital may be of some value.[67] [68] [69]

» Vigabatrin may cause permanent vision loss and has restricted distribution in some countries.

» Sodium-channel-blocking drugs, such as oxcarbazepine, should be considered optimal therapy when the epileptic encephalopathy is suspected to be due to gain-of-function pathogenic variants of SCN2A/SCN8A or loss-of-function KCNQ2 variants.

» Quinidine has been used to treat epilepsy associated with gain-of-function KCNT1 variants, but studies have yielded contradictory results.[70] [71]

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

**2nd** **ketogenic diet or surgery**

» Ketogenic diets should be considered for patients with refractory epilepsy. Use requires a skilled team including a dietitian, and regular monitoring.[60][61]

» Surgery (resection, disconnection) may be effective if the majority of seizures are focal and due to an identified structural cause. It is important to identify potential structural aetiology and consider surgery early if seizures are refractory to drug treatment.[72]

**infantile epileptic spasms syndrome (IESS) (including West syndrome)**

**1st** **corticosteroid or corticotropin (ACTH) or vigabatrin**

### Primary options

» prednisolone: consult specialist for guidance on dose

**OR**

» corticotropin: consult specialist for guidance on dose

**OR**

MANAGEMENT

## Ongoing

» vigabatrin: consult specialist for guidance on dose

### Secondary options

» prednisolone: consult specialist for guidance on dose
**-or-**
» corticotropin: consult specialist for guidance on dose
**--AND--**
» vigabatrin: consult specialist for guidance on dose

» Epileptic spasms are resistant to most anticonvulsants. An oral corticosteroid, ACTH, or vigabatrin (the treatment of choice for patients with tuberous sclerosis complex) should be used as initial treatment as soon as infantile epileptic spasms are diagnosed, as all have shown efficacy in studies.[73] [74] [75] [76]

» ACTH and corticosteroids have similar reported efficacy: 46% and 44% of patients, respectively, showed a response to treatment in one study. Response rates to vigabatrin were 62% for infants with tuberous sclerosis complex and 29% for those with other causes of infantile spasms.[77] The presence or absence of hypsarrhythmia should not impact treatment decisions.[78]

» Vigabatrin may cause permanent vision loss and has restricted distribution in some countries.

» Recommendations regarding drug regimen, doses, and duration of treatment vary. The most common regimen is ACTH, followed by a corticosteroid (usually prednisolone). Treatment dose may need to be escalated quickly in an attempt to stop spasms and improve electroencephalogram (EEG). A specialist should be consulted for guidance on choice of regimen.

» If the first treatment is ineffective, an alternative medication from the initial options that has a different mechanism of action should be tried, as these are more effective than using standard anticonvulsants: that is, vigabatrin if prednisolone or ACTH was used as the primary option, and prednisolone or ACTH if vigabatrin was used as the primary option.[79] Alternatively, prednisolone or ACTH may be used in combination with vigabatrin; there is some evidence for improved seizure control with

## Ongoing

combination therapy, but no good evidence that it changes long-term outcomes.[80]

**2nd** **alternative anticonvulsants or ketogenic diet or surgery**

» Evidence for the effectiveness of other treatments for refractory IESS is limited. Choice of treatment should be made on an individual patient-specific basis.

» There is insufficient evidence for efficacy of other anticonvulsants for the treatment of refractory infantile spasms. Medications used have included topiramate, clobazam, valproate, zonisamide, levetiracetam, and phenobarbital. Valproate is contraindicated in patients with urea cycle disorders and some mitochondrial disorders, especially those caused by mitochondrial DNA polymerase gamma, and should be avoided in children under age 2 years unless these causes are excluded.[79] [81]

» Pyridoxine is sometimes used as a treatment option, although one study reported that add-on pyridoxine was ineffective.[82] [83] [84]

» Ketogenic diets are an effective option for intractable epileptic spasms.[61] However, effects may be temporary, so use is reserved for hormone-resistant cases. Use requires a skilled team including a dietitian, and regular monitoring.[60] [61]

» For children with drug-resistant epileptic spasms who have localised brain abnormalities (especially when they correlate with EEG localisation), surgery (resection, disconnection) is considered appropriate. Structural abnormalities (e.g., tumours, porencephaly, hemimegalencephaly) are indications for surgery with good potential outcome. Focal cortical dysplasia is also an indication, especially if it correlates with EEG findings. Early surgery is suggested for drug-resistant cases, because early intervention may lead to better cognitive prognosis.

**myoclonic epilepsy in infancy (MEI)**

**1st** **anticonvulsants**

### Primary options

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

### Secondary options

MANAGEMENT

## Ongoing

» clonazepam: children <10 years of age or body weight <30 kg: 0.01 to 0.03 mg/kg/day orally given in 2-3 divided doses initially, increase gradually according to response, maximum 0.2 mg/kg/day; children ≥10 years of age or body weight ≥30 kg: 0.5 mg orally three times daily initially, increase gradually according to response, maximum 20 mg/day

**OR**

» topiramate: consult specialist for guidance on dose

**OR**

» lamotrigine: consult specialist for guidance on dose

**OR**

» levetiracetam: consult specialist for guidance on dose

» Valproate monotherapy is generally considered effective in patients with MEI.[85] [86] Valproate is contraindicated in patients with urea cycle disorders and some mitochondrial disorders, especially those caused by mitochondrial DNA polymerase gamma, and should be avoided in children under age 2 years unless these causes are excluded. Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» Other treatment options include topiramate, lamotrigine, clonazepam, and levetiracetam.[67]

» Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» There is a suggestion that delays in the start of treatment may cause cognitive problems later in life.[87]

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and

## Ongoing

any drug interactions between anticonvulsants and any other drug the patient may be taking.

**Dravet syndrome** **1st** **anticonvulsants**

### Primary options

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

**OR**

» clobazam: children ≥2 years of age and body weight ≤30 kg: 5 mg orally once daily initially, increase gradually according to response, maximum 20 mg/day given in 2 divided doses; children ≥2 years of age and body weight >30 kg: 5 mg orally twice daily initially, increase gradually according to response, maximum 40 mg/day given in 2 divided doses

### Secondary options

» stiripentol: children ≥6 months of age and ≥7 kg body weight: 50 mg/kg/day orally given in 2 divided doses initially, increase gradually according to response, maximum 3000 mg/day

The daily dose may be given in 3 divided doses (rather than 2 divided doses) in patients ≥1 year of age and body weight ≥10 kg.

**-and-**

» clobazam: children ≥2 years of age and body weight ≤30 kg: 5 mg orally once daily initially, increase gradually according to response, maximum 20 mg/day given in 2 divided doses; children ≥2 years of age and body weight >30 kg: 5 mg orally twice daily initially, increase gradually according to response, maximum 40 mg/day given in 2 divided doses

**OR**

» fenfluramine: children ≥2 years of age: 0.1 mg/kg orally twice daily initially, increase gradually according to response, maximum 0.7 mg/kg/day or 26 mg/day

A dose reduction may be required when used with certain drugs (e.g., stiripentol, clobazam); consult your local drug formulary.

## Ongoing

Fenfluramine has restricted distribution in some countries.

### Tertiary options

» cannabidiol (CBD): children ≥1 year of age: 2.5 mg/kg orally twice daily initially, increase gradually according to response, maximum 20 mg/kg/day
Cannabidiol has restricted distribution in some countries.

» Valproate and clobazam are recommended as initial therapies.[21] [88] [89]

» Valproate is contraindicated in patients with urea cycle disorders and some mitochondrial disorders, especially those caused by mitochondrial DNA polymerase gamma, and should be avoided in children under age 2 years unless these causes are excluded. Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» If valproate and clobazam are insufficiently effective, stiripentol and/or fenfluramine should be considered.[21] [88] [89]

» Stiripentol (a cytochrome P450 inhibitor that increases blood levels of other anticonvulsants) is effective when added to clobazam, and when used as monotherapy (off-label). It is approved for use as adjunctive therapy with clobazam for Dravet syndrome in children from age 6 months.[21] [89] [90] Stiripentol may cause neutropenia and thrombocytopenia; haematological testing should be performed before and during treatment.

» Fenfluramine (a serotonin receptor agonist) is approved to treat seizures related to Dravet syndrome in patients aged 2 years and older. It may be used as monotherapy or in combination with other drugs. In randomised controlled trials, fenfluramine resulted in significantly greater reduction in the frequency of convulsive seizures compared with placebo.[21] [91] [92] Fenfluramine is associated with valvular heart disease and pulmonary arterial hypertension; an ECG should be performed before and during treatment.

» Cannabidiol oral solution is approved for the treatment of seizures associated with

## Ongoing

Dravet syndrome for patients aged 1 year and older (2 years and older in some countries). Pharmaceutical-grade cannabidiol is associated with a decrease in the frequency of seizures related to Dravet syndrome, although the mechanism of action is unknown.[93] [94] [95] There is evidence that cannabidiol is effective in the absence as well as in the presence of clobazam.[96] [97] Use cannabidiol with caution in patients with hepatic disease.

» Sodium-channel-blocking drugs such as carbamazepine, oxcarbazepine, lamotrigine, and phenytoin are known to exacerbate seizures in children with Dravet syndrome, and should be avoided.[21] [89]

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

**2nd** **topiramate**

### Primary options

» topiramate: consult specialist for guidance on dose

» Topiramate may be used as monotherapy or adjunctively. Efficacy of topiramate when used as adjunctive therapy has been reported.[21] [98]

**2nd** **ketogenic diet**

» Ketogenic diets are effective, and should be considered after two unsuccessful anticonvulsant trials, or earlier in some cases. Use requires a skilled team including a dietitian, and regular monitoring.[60] [61]

**3rd** **vagus nerve stimulation**

» Vagus nerve stimulation typically results in a <50% reduction in seizures, but should be considered only after other therapeutic options have been tried.[21]

## Ongoing

**genetic epilepsy with febrile seizures plus (GEFS+)**

**1st** **anticonvulsants**

### Primary options

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

**OR**

» lamotrigine: consult specialist for guidance on dose

**OR**

» levetiracetam: consult specialist for guidance on dose

**OR**

» topiramate: consult specialist for guidance on dose

» Seizures typically respond to treatment with anticonvulsants.[31] Treatment options include valproate, lamotrigine, levetiracetam, or topiramate.

» Valproate is contraindicated in patients with urea cycle disorders and some mitochondrial disorders, especially those caused by mitochondrial DNA polymerase gamma, and should be avoided in children under age 2 years unless these causes are excluded. Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and



## Ongoing

any drug interactions between anticonvulsants and any other drug the patient may be taking.

### epilepsy syndromes with onset in childhood (2-12 years)

**epilepsy with myoclonic-atonic seizures (EMAtS; Doose syndrome)**

**1st** **anticonvulsant and/or ketogenic diet**

**Primary options**

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

» Valproate is recommended most often as first-line therapy.[100] [101] Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» Ketogenic diets are highly effective for this syndrome.[101] In one study of a large retrospective multi-centre cohort, therapy with a ketogenic diet was by far the most effective treatment, and it therefore should be considered as initial therapy.[99] Use requires a skilled team including a dietitian, and regular monitoring.[60] [61]

**2nd** **alternative anticonvulsants**

**Primary options**

» clobazam: children ≥2 years of age and body weight ≤30 kg: 5 mg orally once daily initially, increase gradually according to response, maximum 20 mg/day given in 2 divided doses; children ≥2 years of age and body weight >30 kg: 5 mg orally twice daily initially, increase gradually according to response, maximum 40 mg/day given in 2 divided doses

**OR**

» clonazepam: children <10 years of age or body weight <30 kg: 0.01 to 0.03 mg/kg/day orally given in 2-3 divided doses initially, increase gradually according to response, maximum 0.2 mg/kg/day; children ≥10 years of age or body weight ≥30 kg: 0.5 mg orally three times daily initially, increase gradually according to response, maximum 20 mg/day

**OR**

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» levetiracetam: children ≥6 years of age: 20 mg/kg/day orally (immediate-release)/ intravenously initially given in 2 divided doses, increase gradually according to response, maximum 60 mg/kg/day or 3000 mg/day; children ≥16 years of age: 500 mg orally (immediate-release)/intravenously twice daily initially, increase gradually according to response, maximum 3000 mg/day

**OR**

» zonisamide: children 1-15 years of age: consult specialist for guidance on dose; children ≥16 years of age: 100 mg orally once daily initially, increase gradually according to response, maximum 600 mg/day

**OR**

» topiramate: children ≥2 years of age: 1-3 mg/kg orally (immediate-release) once daily initially, increase gradually according to response, maximum 9 mg/kg/day or 400 mg/day

An extended-release formulation is also available; consult your local drug formulary for dose.

### Secondary options

» lamotrigine: consult specialist for guidance on dose

Dose depends on whether the patient is on valproate, an enzyme-inducing anticonvulsant, or any other anticonvulsant, as well as the patient's age and weight.

**OR**

» ethosuximide: children 3-6 years of age: 250 mg orally once daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses; children ≥6 years of age: 250 mg orally twice daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses

Adjust dose according to serum ethosuximide level.

**OR**

## Ongoing

» rufinamide: children ≥1 year of age: 10 mg/kg/day orally given in 2 divided doses initially, increase gradually according to response, maximum 45 mg/kg/day or 3200 mg/day
Lower initial doses are recommended in patients on valproate.

**OR**

» perampanel: children ≥12 years of age: 2-4 mg orally once daily at bedtime initially, increase gradually according to response, maximum 12 mg/day
Dose depends on whether the patient is on a concomitant enzyme-inducing anticonvulsant or not.

**OR**

» felbamate: children 2-14 years of age: 15 mg/kg/day orally given in 3-4 divided doses initially, increase dose gradually according to response, maximum 45 mg/kg/day or 3600 mg/day
A dose reduction of concomitant anticonvulsants may be required.

» Treatments with evidence of effectiveness are benzodiazepines (e.g., clobazam, clonazepam), levetiracetam, zonisamide, and topiramate.[101]

» Lamotrigine, ethosuximide, rufinamide, perampanel, and felbamate also have some evidence of effectiveness.[101]

» Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» Perampanel may cause severe psychiatric and behavioural reactions (e.g., aggression, hostility, homicidal ideation); monitor patients closely during dose titration and at higher doses.

» Felbamate may cause aplastic anaemia or hepatic failure; haematological testing and liver function testing should be performed before and during treatment.

» Vigabatrin and sodium-channel-blocking drugs other than lamotrigine should be avoided.[101]

## Ongoing

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

**3rd** **vagus nerve stimulation or corpus callosotomy**

» Vagus nerve stimulation or corpus callosotomy (for drop attacks) may be considered only if medications and ketogenic diets are insufficiently effective.[101]

**Lennox-Gastaut syndrome (LGS)**

**1st** **anticonvulsants**

### Primary options

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day
**-and/or-**
» clobazam: children ≥2 years of age and body weight ≤30 kg: 5 mg orally once daily initially, increase gradually according to response, maximum 20 mg/day given in 2 divided doses; children ≥2 years of age and body weight >30 kg: 5 mg orally twice daily initially, increase gradually according to response, maximum 40 mg/day given in 2 divided doses

### Secondary options

» lamotrigine: consult specialist for guidance on dose
Dose depends on whether the patient is on valproate, an enzyme-inducing anticonvulsant, or any other anticonvulsant, as well as the patient's age and weight.

**OR**

» topiramate: children ≥2 years of age: 1-3 mg/kg orally (immediate-release) once daily initially, increase gradually according to response, maximum 9 mg/kg/day or 400 mg/day
An extended-release formulation is also available; consult your local drug formulary for dose.

**OR**

## Ongoing

» cannabidiol (CBD): children ≥1 year of age: 2.5 mg/kg orally twice daily initially, increase gradually according to response, maximum 20 mg/kg/day
Cannabidiol has restricted distribution in some countries.

**OR**

» fenfluramine: children ≥2 years of age: 0.1 mg/kg orally twice daily initially, increase gradually according to response, maximum 0.7 mg/kg/day or 26 mg/day
A dose reduction may be required when used with certain drugs; consult your local drug formulary. Fenfluramine has restricted distribution in some countries.

**OR**

» rufinamide: children ≥1 year of age: 10 mg/kg/day orally given in 2 divided doses initially, increase gradually according to response, maximum 45 mg/kg/day or 3200 mg/day
Lower initial doses are recommended in patients on valproate.

### Tertiary options

» levetiracetam: children ≥6 years of age: 20 mg/kg/day orally (immediate-release)/intravenously initially given in 2 divided doses, increase gradually according to response, maximum 60 mg/kg/day or 3000 mg/day; children ≥16 years of age: 500 mg orally (immediate-release)/intravenously twice daily initially, increase gradually according to response, maximum 3000 mg/day

**OR**

» perampanel: children ≥12 years of age: 2-4 mg orally once daily at bedtime initially, increase gradually according to response, maximum 12 mg/day
Dose depends on whether the patient is on a concomitant enzyme-inducing anticonvulsant or not.

**OR**

## Ongoing

» zonisamide: children 1-15 years of age: consult specialist for guidance on dose; children ≥16 years of age: 100 mg orally once daily initially, increase gradually according to response, maximum 600 mg/day

**OR**

» felbamate: children 2-14 years of age: 15 mg/kg/day orally given in 3-4 divided doses initially, increase dose gradually according to response, maximum 45 mg/kg/day or 3600 mg/day
A dose reduction of concomitant anticonvulsants may be required.

**OR**

» lacosamide: children ≥4 years of age and body weight 11-30 kg: 1 mg/kg orally/intravenously twice daily initially, increase gradually according to response, maximum 12 mg/kg/day; children ≥4 years of age and body weight 30-50 kg: 1 mg/kg orally/intravenously twice daily initially, increase gradually according to response, maximum 8 mg/kg/day; children ≥4 years of age and body weight ≥50 kg: 50 mg orally/intravenously twice daily initially, increase gradually according to response, maximum 400 mg/day

**OR**

» brivaracetam: children ≥1 month of age and body weight <11 kg: 0.75 to 1.5 mg/kg orally twice daily initially, increase gradually according to response, maximum 6 mg/kg/day; children ≥1 month of age and body weight 11-20 kg: 0.5 to 1.25 mg/kg orally twice daily initially, increase gradually according to response, maximum 5 mg/kg/day; children ≥1 month of age and body weight 20-50 kg: 0.5 to 1 mg/kg orally twice daily initially, increase gradually according to response, maximum 4 mg/kg/day; children ≥1 month of age and body weight >50 kg: 25-50 mg orally twice daily initially, increase gradually according to response, maximum 200 mg/day

**OR**

» cenobamate: consult specialist for guidance on dose

## Ongoing

» LGS is significantly resistant to therapy, and monotherapy with an anticonvulsant is rarely effective. This often means that polytherapy at high doses is required, which may lead to a paradoxical increase in seizure frequency. Careful discussion with carers about treatment goals is necessary to balance seizure control with medication adverse effects. Goals are typically to decrease the burden of seizures that are prolonged or associated with injury, but seizure freedom is unlikely.

» Valproate is the most commonly used first-line agent. Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» Clobazam may also be considered first line as monotherapy, or in combination with valproate.

» Other anticonvulsants with evidence of effectiveness for treating seizures associated with LGS include rufinamide, lamotrigine, topiramate, cannabidiol, and fenfluramine.[102] [103] [104] [105] [106]

» Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» Cannabidiol oral solution is approved for the treatment of seizures associated with LGS in patients aged 1 year and older (2 years and older in some countries). In randomised, double-blind, placebo-controlled trials, adjunctive cannabidiol oral solution effectively reduced the frequency of drop seizures compared with placebo.[104] [107] [108][109] There is some evidence that cannabidiol is effective in the absence as well as in the presence of clobazam.[96] [97] Adverse effects of cannabidiol include elevated liver enzymes, gastrointestinal intolerance, and sleep disturbances.[94] [110] Use cannabidiol with caution in patients with hepatic disease.

» Fenfluramine is approved for the treatment of seizures associated with LGS in patients aged 2 years and older. One randomised controlled trial and an open-label extension study showed that fenfluramine resulted in a significantly greater reduction in drop seizures than placebo in patients with LGS; this effect appeared to be greatest in patients with generalised tonic-

## Ongoing

clonic seizures.[111] [112] Fenfluramine is associated with valvular heart disease and pulmonary arterial hypertension; an ECG should be performed before and during treatment.

» Other anticonvulsants that may be considered include levetiracetam, perampanel, zonisamide, felbamate, lacosamide, brivaracetam, and cenobamate (not licensed for use in children), although in some cases evidence of effectiveness in LGS is scarce or uncertain.[102] [104][105] [113]

» Perampanel may cause severe psychiatric and behavioural reactions (e.g., aggression, hostility, homicidal ideation); monitor patients closely during dose titration and at higher doses.

» Felbamate may cause aplastic anaemia or hepatic failure; haematological testing and liver function testing should be performed before and during treatment.

» Carbamazepine, eslicarbazepine, gabapentin, oxcarbazepine, phenytoin, pregabalin, and vigabatrin may exacerbate seizures associated with LGS, and so are usually avoided.[105]

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

**adjunct** **corticotropin (ACTH) and/or corticosteroid**

Treatment recommended for SOME patients in selected patient group

» Corticosteroids and/or ACTH may be indicated for short-term adjunctive treatment during a particularly difficult period (i.e., at onset, in status epilepticus, or during a period of significant seizure exacerbation). Recommendations regarding drug regimen, doses, and duration of treatment vary. A specialist should be consulted for guidance on choice of regimen in this age group.

**2nd** **non-pharmacological therapies**

## Ongoing

» Non-pharmacological therapies that may be tried include ketogenic diets, vagus nerve stimulation, corpus callosotomy, or (if there is a dominant and/or structural seizure focus) resective surgery.[61] [104] [114] Use of a ketogenic diet requires a skilled team including a dietitian, and regular monitoring.[60] [61]

**childhood absence epilepsy (CAE)** — **1st** — **anticonvulsants**

### Primary options

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

**OR**

» ethosuximide: children 3-6 years of age: 250 mg orally once daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses; children ≥6 years of age: 250 mg orally twice daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses
Adjust dose according to serum ethosuximide level.

### Secondary options

» lamotrigine: consult specialist for guidance on dose
Dose depends on whether the patient is on valproate, an enzyme-inducing anticonvulsant, or any other anticonvulsant, as well as the patient's age and weight.

**OR**

» levetiracetam: children ≥6 years of age: 20 mg/kg/day orally (immediate-release)/intravenously initially given in 2 divided doses, increase gradually according to response, maximum 60 mg/kg/day or 3000 mg/day; children ≥16 years of age: 500 mg orally (immediate-release)/intravenously twice daily initially, increase gradually according to response, maximum 3000 mg/day

### Tertiary options

» topiramate: children ≥2 years of age: 1-3 mg/kg orally (immediate-release) once daily

## Ongoing

initially, increase gradually according to response, maximum 9 mg/kg/day or 400 mg/day
An extended-release formulation is also available; consult your local drug formulary for dose.

**OR**

» clobazam: children ≥2 years of age and body weight ≤30 kg: 5 mg orally once daily initially, increase gradually according to response, maximum 20 mg/day given in 2 divided doses; children ≥2 years of age and body weight >30 kg: 5 mg orally twice daily initially, increase gradually according to response, maximum 40 mg/day given in 2 divided doses

**OR**

» clonazepam: children <10 years of age or body weight <30 kg: 0.01 to 0.03 mg/kg/day orally given in 2-3 divided doses initially, increase gradually according to response, maximum 0.2 mg/kg/day; children ≥10 years of age or body weight ≥30 kg: 0.5 mg orally three times daily initially, increase gradually according to response, maximum 20 mg/day

**OR**

» perampanel: children ≥12 years of age: 2-4 mg orally once daily at bedtime initially, increase gradually according to response, maximum 12 mg/day
Dose depends on whether the patient is on a concomitant enzyme-inducing anticonvulsant or not.

**OR**

» zonisamide: children 1-15 years of age: consult specialist for guidance on dose; children ≥16 years of age: 100 mg orally once daily initially, increase gradually according to response, maximum 600 mg/day

» Generalised-onset tonic-clonic seizures occur in some absence epilepsies. In this case, treatment should be directed at treating both the tonic-clonic seizures and the absences.[7]

## Ongoing

» In children with absence seizures only, ethosuximide is the first-line option.[115]

» Valproate is the recommended first-line anticonvulsant for patients with both absences and tonic-clonic seizures, but the adverse-effect profile is not as favourable as that of ethosuximide.[115] [116] [117] Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» One Cochrane review supports the use of lamotrigine and levetiracetam as suitable alternatives to valproate, particularly for patients of child-bearing potential for whom valproate may not be an appropriate therapy due to teratogenicity.[116]

» Lamotrigine may be added to valproate therapy, or other polypharmacy may be required, for refractory cases.[27] [118] Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» Topiramate, benzodiazepines (e.g., clobazam, clonazepam), perampanel, and zonisamide are further options.[119] [120] [121]

» Perampanel may cause severe psychiatric and behavioural reactions (e.g., aggression, hostility, homicidal ideation); monitor patients closely during dose titration and at higher doses.

» Gabapentin is not effective in these patients, and evidence suggests that carbamazepine and vigabatrin may exacerbate absence seizures.[122] Therefore, use of these agents is not recommended.[27]

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

## Ongoing

**epilepsy with myoclonic absence (EMA)** — **1st** — **anticonvulsants**

### Primary options

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

**OR**

» ethosuximide: children 3-6 years of age: 250 mg orally once daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses; children ≥6 years of age: 250 mg orally twice daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses
Adjust dose according to serum ethosuximide level.

**OR**

» lamotrigine: consult specialist for guidance on dose
Dose depends on whether the patient is on valproate, an enzyme-inducing anticonvulsant, or any other anticonvulsant, as well as the patient's age and weight.

**OR**

» levetiracetam: children ≥6 years of age: 20 mg/kg/day orally (immediate-release)/intravenously initially given in 2 divided doses, increase gradually according to response, maximum 60 mg/kg/day or 3000 mg/day; children ≥16 years of age: 500 mg orally (immediate-release)/intravenously twice daily initially, increase gradually according to response, maximum 3000 mg/day

**OR**

» clobazam: children ≥2 years of age and body weight ≤30 kg: 5 mg orally once daily initially, increase gradually according to response, maximum 20 mg/day given in 2 divided doses; children ≥2 years of age and body weight >30 kg: 5 mg orally twice daily initially, increase gradually according

## Ongoing

to response, maximum 40 mg/day given in 2 divided doses

**OR**

» clonazepam: children <10 years of age or body weight <30 kg: 0.01 to 0.03 mg/kg/day orally given in 2-3 divided doses initially, increase gradually according to response, maximum 0.2 mg/kg/day; children ≥10 years of age or body weight ≥30 kg: 0.5 mg orally three times daily initially, increase gradually according to response, maximum 20 mg/day

» EMA is often refractory to anticonvulsants, and combinations of drugs (polypharmacy) may be required.

» Medications commonly used include valproate, ethosuximide, lamotrigine, levetiracetam, and benzodiazepines (e.g., clobazam, clonazepam).[116] [123]

» Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

**epilepsy with eyelid myoclonia (EEM)** — **1st** — **anticonvulsants**

**Primary options**

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

**OR**

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» lamotrigine: consult specialist for guidance on dose
Dose depends on whether the patient is on valproate, an enzyme-inducing anticonvulsant, or any other anticonvulsant, as well as the patient's age and weight.

**OR**

» levetiracetam: children ≥6 years of age: 20 mg/kg/day orally (immediate-release)/intravenously initially given in 2 divided doses, increase gradually according to response, maximum 60 mg/kg/day or 3000 mg/day; children ≥16 years of age: 500 mg orally (immediate-release)/intravenously twice daily initially, increase gradually according to response, maximum 3000 mg/day

### Secondary options

» ethosuximide: children 3-6 years of age: 250 mg orally once daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses; children ≥6 years of age: 250 mg orally twice daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses
Adjust dose according to serum ethosuximide level.

**OR**

» clobazam: children ≥2 years of age and body weight ≤30 kg: 5 mg orally once daily initially, increase gradually according to response, maximum 20 mg/day given in 2 divided doses; children ≥2 years of age and body weight >30 kg: 5 mg orally twice daily initially, increase gradually according to response, maximum 40 mg/day given in 2 divided doses

» This syndrome tends to be resistant to drug therapy, with up to 80% of patients developing medically intractable epilepsy and requiring polypharmacy. Generalised tonic-clonic seizures are often responsive to treatment, while eyelid myoclonia are not fully controlled.[32]

» Valproate, lamotrigine, and levetiracetam are recommended as first-line treatment

## Ongoing

options, and may reduce seizures by more than 50%.[124] [125] [126] Levetiracetam and lamotrigine should particularly be considered for patients of child-bearing potential due to the teratogenic risks of valproate.[124] [125]

» Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» There is some evidence for effectiveness of ethosuximide and clobazam.[124] [125]

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

**adjunct** **lens therapy**

Treatment recommended for SOME patients in selected patient group

» Lens therapy may be trialled for patients with a photoparoxysmal response, although evidence for effectiveness is limited.[124] [125]

**2nd** **alternative anticonvulsants and/or ketogenic diet**

» There is no consensus for other treatments for EEM.[124]

» Other anticonvulsant medication (e.g., topiramate, brivaracetam, zonisamide, cannabidiol, fenfluramine, clonazepam, perampanel, lacosamide, and acetazolamide) may be tried, but there is little evidence for effectiveness in EEM.[124] [125]

» Cannabidiol can worsen seizures, especially eyelid myoclonia, and should be used with caution.[125]

## Ongoing

» Sodium-channel-blocking drugs, except for lamotrigine, may worsen seizures and should be avoided.[124] [125]

» Data on the use of ketogenic diets in EEM are limited.[124] [125] Use of a ketogenic diet requires a skilled team including a dietitian, and regular monitoring.[60] [61]

**adjunct** **lens therapy**

Treatment recommended for SOME patients in selected patient group

» Lens therapy may be trialled for patients with a photoparoxysmal response, although evidence for effectiveness is limited.[124] [125]

### epilepsy syndromes with onset at a variable age

**epilepsy with generalised tonic-clonic seizures alone (GTCA)**

**1st** **anticonvulsants**

#### Primary options

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

#### Secondary options

» lamotrigine: consult specialist for guidance on dose
Dose depends on whether the patient is on valproate, an enzyme-inducing anticonvulsant, or any other anticonvulsant, as well as the patient's age and weight.

**OR**

» levetiracetam: children ≥6 years of age: 20 mg/kg/day orally (immediate-release)/intravenously initially given in 2 divided doses, increase gradually according to response, maximum 60 mg/kg/day or 3000 mg/day; children ≥16 years of age: 500 mg orally (immediate-release)/intravenously twice daily initially, increase gradually according to response, maximum 3000 mg/day

#### Tertiary options

» topiramate: children ≥2 years of age: 1-3 mg/kg orally (immediate-release) once daily initially, increase gradually according to response, maximum 9 mg/kg/day or 400 mg/day

## Ongoing

An extended-release formulation is also available; consult your local drug formulary for dose.

**OR**

» clobazam: children ≥2 years of age and body weight ≤30 kg: 5 mg orally once daily initially, increase gradually according to response, maximum 20 mg/day given in 2 divided doses; children ≥2 years of age and body weight >30 kg: 5 mg orally twice daily initially, increase gradually according to response, maximum 40 mg/day given in 2 divided doses

**OR**

» perampanel: children ≥12 years of age: 2-4 mg orally once daily at bedtime initially, increase gradually according to response, maximum 12 mg/day
Dose depends on whether the patient is on a concomitant enzyme-inducing anticonvulsant or not.

» Age at onset is typically between 10 and 25 years (range 5-40 years).[7]

» First-line treatment is valproate.[116] Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» One Cochrane review supports the use of lamotrigine and levetiracetam as suitable alternatives to valproate, particularly for patients of child-bearing potential, for whom valproate may not be an appropriate therapy due to teratogenicity.[116] Lamotrigine is also effective as an adjunctive therapy in controlling primary generalised tonic-clonic seizures.[128] Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» Clobazam and topiramate (monotherapy or with valproate) are also effective options.[129] [130] [131]

» Perampanel is well tolerated and improves control of drug-resistant primary generalised tonic-clonic seizures in idiopathic generalised

## Ongoing

epilepsy when used adjunctively in patients aged 12 years or older.[120] [142] Perampanel may cause severe psychiatric and behavioural reactions (e.g., aggression, hostility, homicidal ideation); monitor patients closely during dose titration and at higher doses.

» Carbamazepine may aggravate seizures in patients with idiopathic generalised epilepsies and so is not recommended.[27]

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

**adjunct** **lifestyle modifications**

Treatment recommended for SOME patients in selected patient group

» Lifestyle changes may need to be implemented to achieve freedom from seizures.

» Patients should be warned of common seizure precipitants, including sleep deprivation with early waking and alcohol consumption.[127]

**2nd** **vagus nerve stimulation or ketogenic diet**

» Vagus nerve stimulation and ketogenic diets are treatment options for patients with drug-resistant idiopathic generalised epilepsy.[58] [61] [133] Use of a ketogenic diet requires a skilled team including a dietitian, and regular monitoring.[60] [61]

**adjunct** **lifestyle modifications**

Treatment recommended for SOME patients in selected patient group

» Lifestyle changes may need to be implemented to achieve freedom from seizures.

» Patients should be warned of common seizure precipitants, including sleep deprivation with early waking and alcohol consumption.[127]

**juvenile myoclonic epilepsy (JME)**

**1st** **anticonvulsants**

**Primary options**

 

## Ongoing

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

### Secondary options

» lamotrigine: consult specialist for guidance on dose
Dose depends on whether the patient is on valproate, an enzyme-inducing anticonvulsant, or any other anticonvulsant, as well as the patient's age and weight.

**OR**

» levetiracetam: children 1-12 years of age: consult specialist for guidance on dose; children ≥12 years of age: 500 mg orally (immediate-release)/intravenously twice daily initially, increase gradually according to response, maximum 3000 mg/day

### Tertiary options

» topiramate: children ≥2 years of age: 1-3 mg/kg orally (immediate-release) once daily initially, increase gradually according to response, maximum 9 mg/kg/day or 400 mg/day
An extended-release formulation is also available; consult your local drug formulary for dose.

**OR**

» zonisamide: children 1-15 years of age: consult specialist for guidance on dose; children ≥16 years of age: 100 mg orally once daily initially, increase gradually according to response, maximum 600 mg/day

**OR**

» perampanel: children ≥12 years of age: 2-4 mg orally once daily at bedtime initially, increase gradually according to response, maximum 12 mg/day
Dose depends on whether the patient is on a concomitant enzyme-inducing anticonvulsant or not.

» Age at onset is typically between 10 and 24 years (range 8-40 years).[7]

## Ongoing

» First-line option is valproate.[116] It may be used alone or in combination with lamotrigine in resistant cases.[116] [134] Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» One Cochrane review supports the use of lamotrigine and levetiracetam as suitable alternatives to valproate, particularly for patients of child-bearing potential, for whom valproate may not be an appropriate therapy due to teratogenicity.[116]

» Levetiracetam is considered the most safe and efficacious of the newer anticonvulsants when used as monotherapy.[135] [136] [137]

» Monotherapy with lamotrigine is controversial as, despite its efficacy in controlling tonic-clonic seizures and absences, there is a very high risk of aggravation of myoclonic jerks.[138] Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» Additional treatment options include topiramate, zonisamide, and perampanel.[120] [139] [140] Perampanel may cause severe psychiatric and behavioural reactions (e.g., aggression, hostility, homicidal ideation); monitor patients closely during dose titration and at higher doses.

» Carbamazepine may aggravate seizures in patients with idiopathic generalised epilepsies and so is not recommended.[27]

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

**adjunct** **lifestyle modifications**

Treatment recommended for SOME patients in selected patient group



 

## Ongoing

» Lifestyle changes may need to be implemented to achieve freedom from seizures.

» Patients should be warned of common seizure precipitants, including sleep deprivation with early waking and alcohol consumption.[127]

**juvenile absence epilepsy (JAE)** — **1st** — **anticonvulsants**

### Primary options

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

**OR**

» ethosuximide: children 3-6 years of age: 250 mg orally once daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses; children ≥6 years of age: 250 mg orally twice daily initially, increase gradually according to response, maximum 20 mg/kg/day or 1500 mg/day given in 2 divided doses
Adjust dose according to serum ethosuximide level.

### Secondary options

» lamotrigine: consult specialist for guidance on dose
Dose depends on whether the patient is on valproate, an enzyme-inducing anticonvulsant, or any other anticonvulsant, as well as the patient's age and weight.

**OR**

» levetiracetam: children 1-12 years of age: consult specialist for guidance on dose; children ≥12 years of age: 500 mg orally (immediate-release)/intravenously twice daily initially, increase gradually according to response, maximum 3000 mg/day

### Tertiary options

» clobazam: children ≥2 years of age and body weight ≤30 kg: 5 mg orally once daily initially, increase gradually according to response, maximum 20 mg/day given in 2 divided doses; children ≥2 years of age and body weight >30 kg: 5 mg orally twice

## Ongoing

daily initially, increase gradually according to response, maximum 40 mg/day given in 2 divided doses

**OR**

» topiramate: children ≥2 years of age: 1-3 mg/kg orally (immediate-release) once daily initially, increase gradually according to response, maximum 9 mg/kg/day or 400 mg/day
An extended-release formulation is also available; consult your local drug formulary for dose.

**OR**

» zonisamide: children 1-15 years of age: consult specialist for guidance on dose; children ≥16 years of age: 100 mg orally once daily initially, increase gradually according to response, maximum 600 mg/day

**OR**

» perampanel: children ≥12 years of age: 2-4 mg orally once daily at bedtime initially, increase gradually according to response, maximum 12 mg/day
Dose depends on whether the patient is on a concomitant enzyme-inducing anticonvulsant or not.

» Age at onset is typically between 9 and 13 years (range 8-20 years).[7]

» First-line anticonvulsant is ethosuximide for patients with absence seizures only. If seizures persist with ethosuximide or if there are generalised tonic-clonic seizures, valproate is preferred.[116] [141] Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» One Cochrane review supports the use of lamotrigine and levetiracetam as suitable alternatives to valproate, particularly for patients of child-bearing potential, for whom valproate may not be an appropriate therapy due to teratogenicity.[116]

## Ongoing

» Additional treatment options include clobazam, topiramate, zonisamide, and perampanel.[120] [141] [142] Perampanel may cause severe psychiatric and behavioural reactions (e.g., aggression, hostility, homicidal ideation); monitor patients closely during dose titration and at higher doses.

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

**adjunct** **lifestyle modifications**

Treatment recommended for SOME patients in selected patient group

» Lifestyle changes may need to be implemented to achieve freedom from seizures.

» Patients should be warned of common seizure precipitants, including sleep deprivation with early waking and alcohol consumption.[127]

**unidentified epilepsy syndrome**

**1st** **anticonvulsants**

**Primary options**

» sodium valproate: 10-15 mg/kg/day orally given in 1-3 divided doses initially, increase gradually according to response, maximum 60 mg/kg/day

**OR**

» lamotrigine: consult specialist for guidance on dose
Dose depends on whether the patient is on valproate, an enzyme-inducing anticonvulsant, or any other anticonvulsant, as well as the patient's age and weight.

**OR**

» levetiracetam: children 1-12 years of age: consult specialist for guidance on dose;

## Ongoing

children ≥12 years of age: 500 mg orally (immediate-release)/intravenously twice daily initially, increase gradually according to response, maximum 3000 mg/day

**OR**

» topiramate: children ≥2 years of age: 1-3 mg/kg orally (immediate-release) once daily initially, increase gradually according to response, maximum 9 mg/kg/day or 400 mg/day
An extended-release formulation is also available; consult your local drug formulary for dose.

### Secondary options

» carbamazepine: children <6 years of age: 10-20 mg/kg/day orally (immediate-release) given in 2-4 divided doses initially, increase gradually according to response, maximum 35 mg/kg/day; children 6-12 years of age: 100 mg orally (immediate-release) twice daily initially, increase gradually according to response, maximum 1000 mg/day given in 2-4 divided doses; children ≥12 years of age: 200 mg orally (immediate-release) twice daily initially, increase gradually according to response, maximum 1200 mg/day given in 2-4 divided doses
Adjust dose according to serum carbamazepine level. An extended-release formulation is also available; consult your local drug formulary for dose.

### Tertiary options

» perampanel: children ≥12 years of age: 2-4 mg orally once daily at bedtime initially, increase gradually according to response, maximum 12 mg/day
Dose depends on whether the patient is on a concomitant enzyme-inducing anticonvulsant or not.

» Sometimes an epileptic syndrome cannot be diagnosed. Anticonvulsant therapy must be tailored to the individual patient, and is based on seizure types, age, sex, and comorbidities. Monotherapy is preferable, although polypharmacy may be required for seizure control if monotherapy is insufficiently effective. A careful balance of seizure control

## Ongoing

and anticonvulsant adverse effects should be maintained.[45]

» If seizures are generalised or it is not known whether they are focal or generalised, broad-spectrum anticonvulsants are recommended. First-line options include valproate, lamotrigine, levetiracetam, and topiramate.

» Valproate is better tolerated than topiramate and more efficacious than lamotrigine, and remains the drug of choice for many patients with generalised and unclassified epilepsies.[143] Valproate may cause serious or fatal hepatic failure (children <2 years of age are at increased risk); hepatic function testing should be performed before and during treatment. Valproate may also cause life-threatening pancreatitis.

» Lamotrigine is also effective as an adjunctive therapy in combination with other anticonvulsants in controlling primary generalised tonic-clonic seizures.[128] [134] Lamotrigine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis).

» Topiramate is well tolerated and effective for prolonged tonic-clonic seizures when used adjunctively with another anticonvulsant, or for resistant tonic-clonic seizures when used as monotherapy.[144] [145]

» Carbamazepine is indicated for generalised tonic-clonic seizures, but can aggravate absence, myoclonic, and tonic/atonic seizures.[146] Carbamazepine may cause serious and life-threatening dermatological reactions (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis), particularly in patients with the HLA-B*1502 allele (which is found mainly in Asian patients). Testing for HLA-B*1502 is recommended in patients with genetically at-risk ancestry before starting treatment. Carbamazepine may cause aplastic anaemia or agranulocytosis, and haematological testing should be performed before and during treatment.

» Perampanel is well tolerated and improves control of drug-resistant primary generalised tonic-clonic seizures in idiopathic generalised epilepsy when used adjunctively in patients aged 12 years or older.[120] [142] Perampanel may cause severe psychiatric and behavioural reactions (e.g., aggression, hostility, homicidal

## Ongoing

ideation); monitor patients closely during dose titration and at higher doses.

» For patients with the potential to become pregnant, see 'Considerations for patients of child-bearing potential' in Management approach .

» Patients may need monotherapy or combination therapy. The list of drugs here reflects options that may be used; however, combinations of these drugs may be required in practice. It is important to take into account any drug interactions between anticonvulsants, and any drug interactions between anticonvulsants and any other drug the patient may be taking.

# Emerging

## Ganaxolone

Ganaxolone is a neurosteroid that acts through positive allosteric modulation of gamma-aminobutyric acid A receptor sites. It is approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of seizures (in children >2 years of age) associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder, which is associated with both generalised and focal seizures.[149] [150]

## Soticlestat

Soticlestat is an investigational selective inhibitor of the brain-specific enzyme cholesterol 24-hydroxylase. In a randomised, double-blind, placebo-controlled study including children with Dravet syndrome or Lennox-Gastaut syndrome, soticlestat was associated with statistically significant, clinically meaningful reductions from baseline in median seizure frequency (combined patient population) and in convulsive seizure frequency (Dravet syndrome cohort). Treatment-emergent adverse events were mostly mild or moderate in severity, and their incidence was similar between the soticlestat and placebo groups.[151]

## Lorcaserin

Lorcaserin is a selective serotonin receptor (5-HT2C) agonist with receptors limited to the central nervous system. It was previously licensed for the management of obesity, but was withdrawn from the market owing to a safety signal of an increased risk of cancer in a long-term study. It is currently in clinical development for the treatment of epilepsy. One retrospective case series reported that lorcaserin may reduce motor seizures in children and young adults with treatment-resistant epilepsies, including Dravet syndrome and Lennox-Gastaut syndrome.[152] Phase 3 clinical trials are under way to assess the efficacy and safety of lorcaserin as adjunctive treatment for Dravet syndrome.[153]

## Carisbamate

Carisbamate has been granted orphan drug designation by the FDA for the potential treatment of seizures associated with Lennox-Gastaut syndrome.[114] Clinical trials are ongoing.[154] [155] [156]

## Retigabine (XEN496)

XEN496, a novel granular paediatric formulation of retigabine (a previously discontinued anticonvulsant), is being investigated for the treatment of patients with KCNQ2 developmental and epileptic encephalopathy.[157] [158]

## Gene therapies

Gene therapies are being investigated for treating Dravet syndrome and Lennox-Gastaut syndrome.[159] [160] For example, STK-001 is an antisense oligonucleotide that is intended to increase the level of productive SCN1A mRNA and consequently increase the expression of the sodium channel protein Nav1.1 in patients with Dravet syndrome.[161] [162]

## Neurostimulation

Deep brain stimulation and responsive neurostimulation therapy have been shown to be effective in adults with refractory epilepsy, but they are not approved for children and evidence in this population is limited.[163] [164] [165] Non-invasive methods such as transcranial magnetic stimulation and transcranial direct current stimulation are being investigated, but information regarding use for treating generalised seizures is scarce.[166] [167]

# Primary prevention

Several causes of childhood epilepsy are potentially preventable, including perinatal insults, traumatic brain injury (TBI), and central nervous system (CNS) infection. Perinatal insult and TBI cause a similar proportion of epilepsies in high-income countries and lower- and middle-income countries, whereas CNS infection is a more common cause in lower- and middle-income countries. Public health measures aimed at preventing epilepsy include maternal and child health care, immunisations, public sanitation, and brain injury prevention. [10]

# Secondary prevention

Patients and their families should be comprehensively informed about possible precipitating factors or triggers that could exacerbate seizures, and if possible try to avoid them. Sleep deprivation and alcohol are well-known precipitants of seizures in children with juvenile myoclonic epilepsy and epilepsy with generalised tonic-clonic seizures alone.[7] Precipitating factors vary from one patient to another, and the patient and/or their family and carers need to be aware of these. Examples of triggers include stress, boredom, photosensitivity, tiredness, sudden noise or startle, fever, physical activity, and changes in environmental temperature.[7][31] [32]

# Patient discussions

Parents and children (if old enough) should be fully informed about their condition, the causes, the importance of preventative therapy, adverse effects they may expect and when to report them, and how to manage a seizure if one does occur. This should be explained to children in terms that they understand.[27]

Patients and/or parents should be encouraged to keep a detailed calendar of any seizures that occur, with a brief description of any possible precipitating factors, length of seizure, characteristics of seizure, post-ictal phenomena, and any changes in treatment (e.g., dose escalations, changes in drugs).

If a generic bioequivalent anticonvulsant drug replaces a brand product, parents and patients should be reassured about equivalent effectiveness, and informed if there are any changes in colour or shape.[182]

Support and communication are essential for the child and their family.[27] [127] Various education and counselling programmes for children with epilepsy and parents exist, but there is insufficient evidence to recommend one over another.[183] A multi-disciplinary team approach is key, with involvement of doctors, nurses, pharmacists, physiotherapists, psychologists, social workers, education specialists, and support groups. It is vital to ensure that each child receives regular coordinated reviews of their epilepsy management.[27] Education of parents, teachers, and peers can minimise the impact of the condition on the patient's quality of life. [Epilepsy Society (UK)] (https://epilepsysociety.org.uk) [Epilepsy Foundation] (https://www.epilepsy.com)

To minimise the risk of injuries and death, general recommendations for everyday life include:

- Young children should not be left in the bath alone.
- Bathroom or bedroom doors should be left unlocked.
- Fireplaces and cookers should be shielded.
- Contact sports should be avoided. Other sports and swimming are possible but should take place under the supervision of instructors or trainers who have been trained in what to do in case of a seizure.
- Driving may need to be restricted or forbidden; this is regulated by law and varies from country to country.

- Level of risk of seizure recurrence associated with sleep deprivation or alcohol consumption should be discussed.

Unnecessary restrictions should be avoided.

If discontinuation of anticonvulsant medication is being considered for patients who have been seizure-free for 18-24 months and who do not have an electroclinical syndrome suggesting otherwise, discuss the risks and benefits of discontinuation with the patient and their family, including the risks of seizure recurrence and treatment resistance. Individual patient characteristics and preferences, including quality of life considerations, should be taken into account.[147]

Contraception and pregnancy

Education about effective contraceptive options and potential adverse pregnancy outcomes should start in early adolescence and continue throughout a patient's reproductive life. Puberty may be associated with increased seizure activity, and patients with epilepsy are more likely to experience anovulatory cycles and irregular menstrual bleeding.[48]

Patients of child-bearing potential should be informed that they must follow a pregnancy prevention programme while on treatment with valproate medicines. For EU countries, the European Medicines Agency states that this programme should include:[49]

- An assessment of the patient's potential for becoming pregnant
- Pregnancy tests before starting and during treatment as needed
- Counselling about the risks of valproate treatment and the need for effective contraception throughout treatment
- A review of ongoing treatment by a specialist at least annually
- A risk acknowledgement form that patients and prescribers will go through at each such annual review to confirm that appropriate advice has been given and understood.

# Monitoring

## Monitoring

Every child with epilepsy should be seen by a specialist at least once per year, but frequency may be as often as every 3 months depending on the child's circumstances.[27] Each child should have a comprehensive individualised care plan that is agreed on by the patient (if old enough), the family, the primary care practitioner, and the specialist.

When epilepsy is well controlled, the only necessary monitoring is for continued control of seizures and adverse effects of medication. Special attention should be paid to sedative adverse effects, which are especially difficult to determine in infants and mentally impaired children.[45]

Regular screening of cognition, behaviour, and mood is recommended for children with epilepsy.[127] [176]

Serum drug level monitoring is not routinely recommended, but may be useful in cases of drug-resistant seizures, when toxic effects are suspected, when pharmacokinetic interactions may have an influence on efficacy, or when comorbidities may alter the drug's metabolism.[27] Baseline measurement and regular monitoring of various parameters (i.e., LFTs, FBC) may be helpful in monitoring for adverse effects associated with some anticonvulsants (e.g., valproate, carbamazepine) and for patients taking enzyme-inducing anticonvulsants.

Abnormal electroencephalogram (EEG) can be a predictor of relapse, although some authors report prolonged remissions despite remaining paroxysmal activity. Therefore, EEG has a secondary role in regulating medical treatment, and there are no strict regulations on how often it should be obtained.

Patients who achieve seizure freedom may eventually wish to discontinue anticonvulsant medications. See 'Drug discontinuation' in Management approach .

FOLLOW UP

# Complications

| Complications | Timeframe | Likelihood |
|---|---|---|
| **worsening seizures** | **short term** | **low** |
| Particular anticonvulsants can worsen seizures.<br><br>Most commonly occurs when underlying syndrome is unknown or wrongly diagnosed and an inappropriate anticonvulsant is initiated.<br><br>Rarely occurs in correctly diagnosed and treated patients. | | |
| **developmental delay** | **long term** | **low** |
| Developmental delay and intellectual disability in children with epilepsy may be due to drug toxicity, socio-psychological factors, status epilepticus, and continuous or long-lasting periods of epileptic activity detected on electroencephalogram without clinical seizures occurring in children with some syndromes (e.g., infantile epileptic spasms syndrome, Lennox-Gastaut syndrome) and epileptic encephalopathies.[3] | | |
| **neurodevelopmental conditions** | **variable** | **medium** |
| Neurodevelopmental conditions occur in many children with epilepsy, and attention, internalising, and thought problems may be specific to epilepsy. ADHD is more prevalent among the paediatric epilepsy population than among children and adolescents without epilepsy. Improved early identification of children with epilepsy at risk for these conditions, evidence-based treatment, and multi-disciplinary management strategies are required to optimise patient management.[176] | | |
| **mood disorders** | **variable** | **medium** |
| Mood disorders (e.g., depression, anxiety) are common among people with epilepsy and can negatively impact on seizure outcome and quality of life.[177] [178]<br><br>Anticonvulsant drugs may be associated with a small increased risk of suicidal thoughts and behaviour. People with epilepsy are also at higher risk of mood and anxiety disorders and suicidal ideation at the time of diagnosis, before starting anticonvulsant medications, and risk of suicide associated with these medications is much lower than the risk of harm due to stopping medications or not starting them.[46] [47]<br><br>Patients should be monitored for mood disorders at each review, and referred for treatment as appropriate.[179] Evidence to inform choice of antidepressant and anticonvulsant drugs in people with epilepsy and depression is very limited.[180] | | |
| **status epilepticus** | **variable** | **low** |
| Status epilepticus is defined as either 5 minutes or more of continuous seizure activity, or two or more discrete seizures between which there is incomplete recovery of consciousness.[171]<br><br>Aim of treatment is to intervene at 5 minutes. Immediate transportation to a medical facility is essential.<br><br>Having an agreed written emergency care plan may significantly improve the outcome in case of prolonged or repeated seizures.<br><br>Benzodiazepines (buccal, rectal, intravenous, or intranasal, depending on drug used) are used first line to treat status epilepticus.[172] [173] Intravenous phenytoin may also be used once the patient is hospitalised. | | |

| Complications | Timeframe | Likelihood |
|---|---|---|
| **sudden unexpected death in epilepsy** | **variable** | **low** |
| Sudden unexpected death (SUDEP) has been reported as the cause of death in 1 in 4500 children annually. The major risk factor for SUDEP is the occurrence of generalised tonic-clonic (GTCS) seizures, and the risk increases in association with increasing frequency of GTCS occurrence.[174]<br><br>Interventions to prevent SUDEP, such as nocturnal supervision (presence of an individual in the bedroom) or special precautions (regular checks throughout the night or the use of a listening device), have been associated with fewer deaths in people with epilepsy, but the evidence is of very low quality, and conclusions cannot be drawn.[175]<br><br>It is important to exclude long QT syndrome as a cause of seizures. There are other cardiac causes (e.g., Brugada syndrome or other genetic cardiac channelopathies) that could cause sudden death. Hence, if the clinical history is suggestive of a cardiac cause (e.g., seizures brought on by exertion, or if there is a family history of sudden death), then a cardiologist should be consulted. | | |
| **evolution into other epilepsy syndromes** | **variable** | **low** |
| Some epileptic syndromes may evolve into another syndrome regardless of the age of the patient and the type of epilepsy they initially have.[3]<br><br>For example, infantile epileptic spasms syndrome may evolve into Lennox-Gastaut syndrome, patients with myoclonic epilepsy in infancy may develop infrequent generalised tonic-clonic seizures, and childhood absence epilepsy may evolve into juvenile absence epilepsy or juvenile myoclonic epilepsy. | | |
| **cardiovascular disease** | **variable** | **low** |
| Certain anticonvulsants, including valproate, carbamazepine, phenobarbital, and phenytoin, as well as the presence of a homozygous 5-methylenetetrahydrofolate reductase polymorphism in the genotype, are potential causes of elevation in plasma homocysteine and serum lipoprotein concentrations. Persistent elevation of these biochemical markers has been shown to be associated with the development of long-term sequelae such as cardiovascular disease, prompting concerns about the long-term implications of chronic anticonvulsant use in children.[181] | | |

# Prognosis

Prognosis varies greatly depending on the epilepsy syndrome, but can also vary for different patients with the same syndrome. There is generally a good prognosis for children with idiopathic epilepsy and late onset of seizures, and in those without neurological dysfunction.[168] Rapid response to therapy is an important predictor of lasting remission. The most important prognostic factor is the aetiology of seizures.[169]

Around one third of all paediatric patients with epilepsy will have a poor long-term outcome in terms of persistent seizures after remission, or no remission at all.[170] Epilepsy with onset in infancy and early childhood often runs a more severe course.[31]

Treatment with anticonvulsants after the first seizure reduces the risk of seizure recurrence, but there is no evidence of a difference when treatment is started after the first versus second seizure in achieving long-term seizure remission.[43]

FOLLOW UP

The risk of relapse after discontinuation of anticonvulsant treatment is higher in patients with brain structural lesions or intellectual disability, and in some epilepsy syndromes (e.g., juvenile myoclonic epilepsy).

# Diagnostic guidelines

## United Kingdom

### Epilepsies in children, young people and adults (https://www.nice.org.uk/guidance/ng217)

**Published by:** National Institute for Health and Care Excellence **Last published:** 2025

## Europe

### EFNS guidelines on the molecular diagnosis of channelopathies, epilepsies, migraine, stroke, and dementias (https://www.ean.org/research/ean-guidelines/guideline-reference-center)

**Published by:** European Academy of Neurology (European Federation of Neurological Societies) **Last published:** 2010

## International

### Methodology for classification and definition of epilepsy syndromes with list of syndromes: report of the ILAE Task Force on Nosology and Definitions (https://www.ilae.org/guidelines/definition-and-classification/classification-and-definition-of-epilepsy-syndromes)

**Published by:** International League Against Epilepsy **Last published:** 2022

### ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: position statement by the ILAE Task Force on Nosology and Definitions (https://www.ilae.org/guidelines/definition-and-classification/classification-and-definition-of-epilepsy-syndromes)

**Published by:** International League Against Epilepsy **Last published:** 2022

### ILAE classification and definition of epilepsy syndromes with onset in childhood: position statement by the ILAE Task Force on Nosology and Definitions (https://www.ilae.org/guidelines/definition-and-classification/classification-and-definition-of-epilepsy-syndromes)

**Published by:** International League Against Epilepsy **Last published:** 2022

### ILAE definition of the idiopathic generalized epilepsy syndromes: position statement by the ILAE Task Force on Nosology and Definitions (https://www.ilae.org/guidelines/definition-and-classification/classification-and-definition-of-epilepsy-syndromes)

**Published by:** International League Against Epilepsy **Last published:** 2022

### International consensus on diagnosis and management of Dravet syndrome (https://onlinelibrary.wiley.com/doi/10.1111/epi.17274)

**Published by:** International DS Consensus Group **Last published:** 2022

### Guidelines for imaging infants and children with recent-onset epilepsy (https://www.ilae.org/guidelines/guidelines-and-reports)

**Published by:** International League Against Epilepsy Subcommittee for Paediatric Neuroimaging **Last published:** 2009

## North America

### ACR appropriateness criteria: seizures and epilepsy (https://www.acr.org/Clinical-Resources/ACR-Appropriateness-Criteria)

**Published by:** American College of Radiology **Last published:** 2019

# Treatment guidelines

## United Kingdom

### Epilepsies in children, young people and adults (https://www.nice.org.uk/guidance/ng217)

**Published by:** National Institute for Health and Care Excellence **Last published:** 2025

## International

### International consensus on diagnosis and management of Dravet syndrome (https://onlinelibrary.wiley.com/doi/10.1111/epi.17274)

**Published by:** International DS Consensus Group **Last published:** 2022

### Epilepsy, seizures, physical exercise, and sports: a report from the ILAE Task Force on Sports and Epilepsy (https://onlinelibrary.wiley.com/doi/full/10.1111/epi.13261)

**Published by:** International League against Epilepsy **Last published:** 2016

### Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes (https://www.ilae.org/guidelines/guidelines-and-reports)

**Published by:** International League Against Epilepsy **Last published:** 2013

## North America

### Antiseizure medication withdrawal in seizure-free patients: practice advisory update summary (https://www.aan.com/Guidelines/Home/Search?topic=Epilepsy)

**Published by:** American Academy of Neurology **Last published:** 2021

### Gynecologic management of adolescents and young women with seizure disorders (https://www.acog.org/clinical/clinical-guidance/committee-opinion)

**Published by:** American College of Obstetricians and Gynecologists **Last published:** 2020 (re-affirmed 2024)

### Efficacy and tolerability of the new antiepileptic drugs I: treatment of new-onset epilepsy (https://www.aan.com/Guidelines/Home/Search?topic=Epilepsy)

**Published by:** American Academy of Neurology; American Epilepsy Society **Last published:** 2018 (re-affirmed 2024)

### Practice guideline: sudden unexpected death in epilepsy incidence rates and risk factors (https://www.aan.com/Guidelines/Home/Search?topic=Epilepsy)

**Published by:** American Academy of Neurology; American Epilepsy Society **Last published:** 2017 (re-affirmed 2023)

### Vagus nerve stimulation for the treatment of epilepsy (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3806910)

**Published by:** American Academy of Neurology **Last published:** 2013 (re-affirmed 2019)

### Practice parameter: treatment of the child with a first unprovoked seizure (https://www.aan.com/Guidelines/Home/Search?topic=Epilepsy)

**Published by:** American Academy of Neurology; Practice Committee of the Child Neurology Society **Last published:** 2003 (re-affirmed 2024)

# Online resources

1. ILAE: EpilepsyDiagnosis.org (https://www.epilepsydiagnosis.org) *(external link)*
2. Epilepsy Society (UK) (https://epilepsysociety.org.uk) *(external link)*
3. Epilepsy Foundation (https://www.epilepsy.com) *(external link)*

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- Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the International League Against Epilepsy: position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017 Apr;58(4):522-30. Full text (https://onlinelibrary.wiley.com/doi/full/10.1111/epi.13670) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28276060?tool=bestpractice.bmj.com)

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# Images

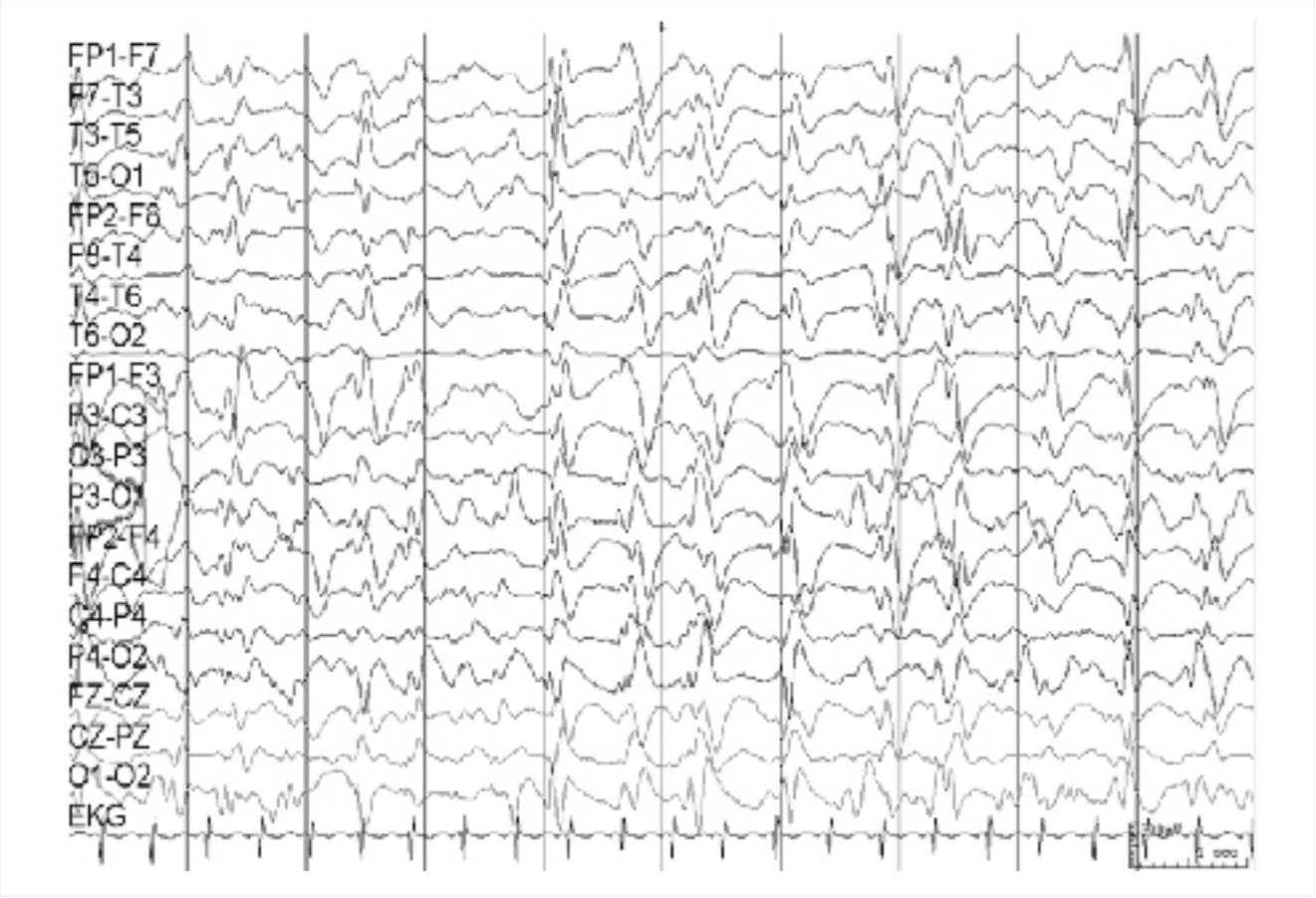


*Figure 1: Electroencephalogram (EEG): epilepsy with myoclonic-atonic seizures*

*Courtesy of Professor Eric Kossoff; used with permission*



 

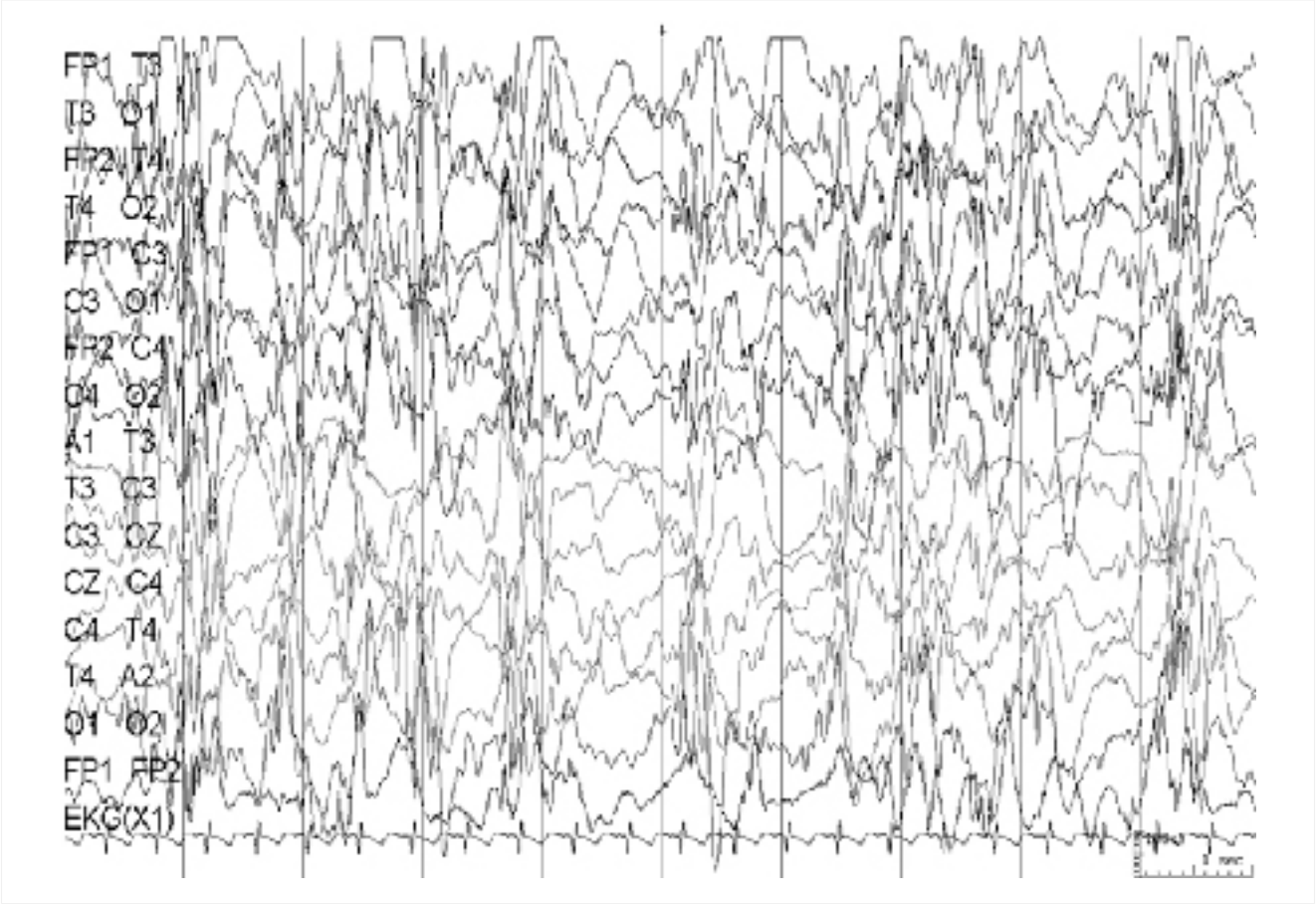


*Figure 2: Electroencephalogram (EEG): Lennox-Gastaut syndrome*

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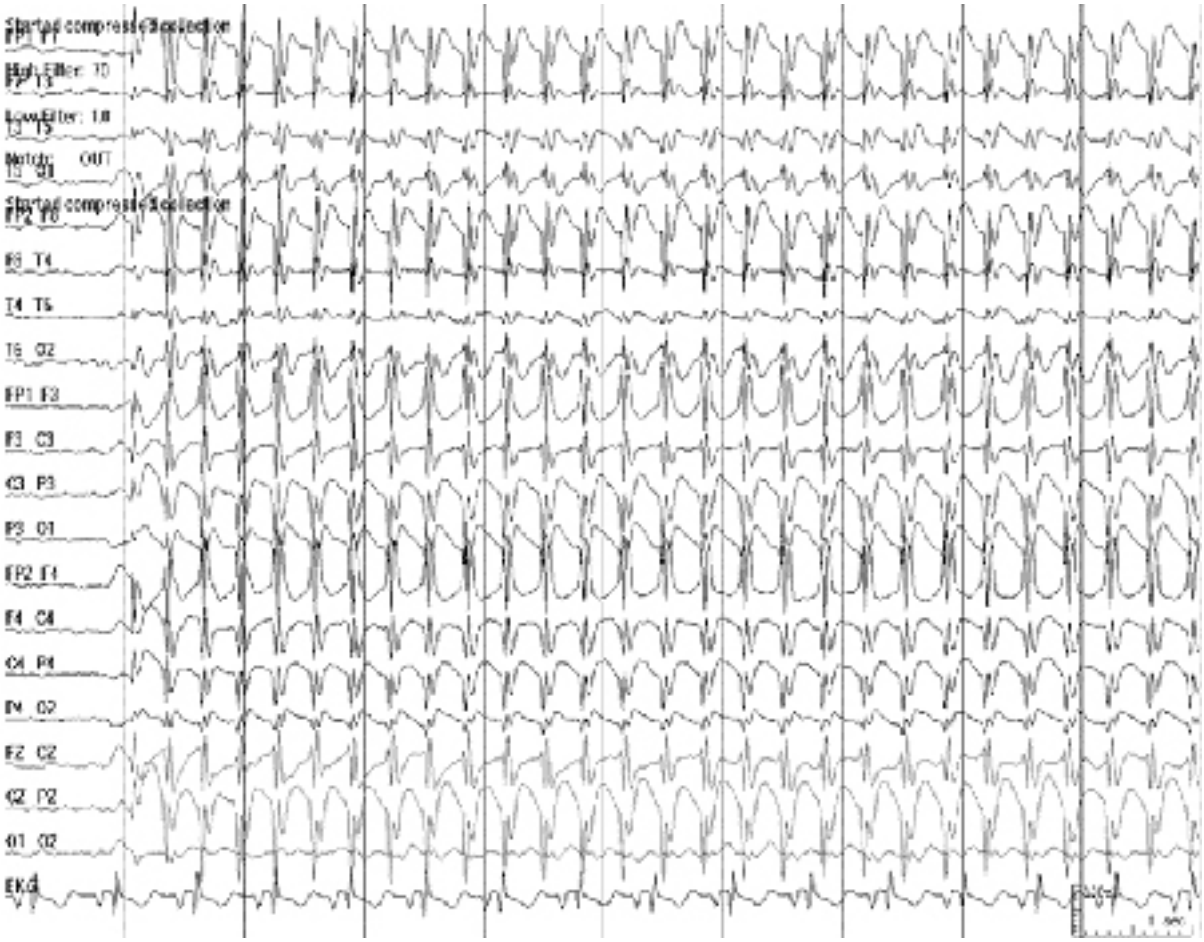

*Figure 3: Electroencephalogram (EEG): childhood absence epilepsy; shows typical 3 per second spike-and-wave pattern*

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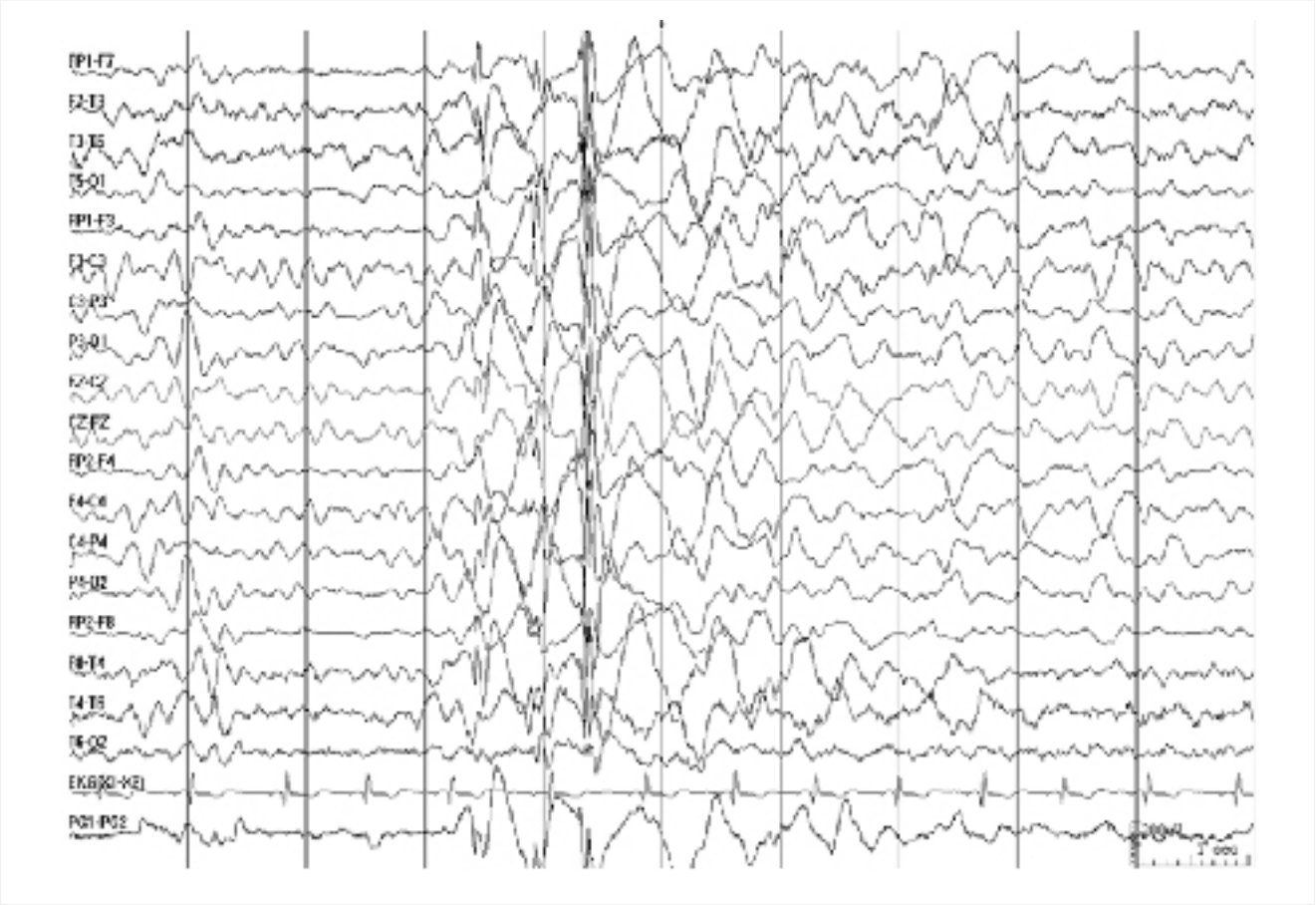

*Figure 4: Electroencephalogram (EEG): juvenile myoclonic epilepsy*

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**Figure 1 – BMJ Best Practice Numeral Style**



 

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DISCLOSURES: AB has previously worked as part of a clinical team with Dr Ewa Posner, a previous contributor to this topic. AB declares that she has no competing interests.