Epilepsy in childhood and adolescence

About two-thirds of children and adolescents with epilepsy respond to treatment with anticonvulsants, and more than half will outgrow their epilepsy.

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Epilepsy is a common problem affecting about 0.5 to 1% of children and adolescents, with the highest incidence rates during the first year of life.[1] Diagnosis largely depends on the clinical history and electroencephalography (EEG). Most children with epilepsy respond well to anticonvulsant treatment.

Definitions and terminology

The terms convulsion, fit and seizure are used interchangeably. An epileptic seizure is caused by an abnormal synchronised electrical discharge from a population of neurons. In children who present with a seizure it is important to first determine whether it was provoked by an acute neurological insult such as head trauma, hypoglycaemia or electrolyte disturbance. A single unprovoked seizure does not constitute a diagnosis of epilepsy. Meta-analysis suggests that the two-year recurrence risk after a first afebrile seizure is only around 40%.[2] Therefore, maintenance anticonvulsants are not usually commenced until a second episode occurs. However, it is important to take a careful history because unrecognised seizures may have preceded the 'index' event in up to half of all cases.[3]

Epilepsy is a group of disorders associated with recurrent unprovoked seizures. Epileptic syndromes are disorders with characteristic seizure types and EEG abnormalities. Sometimes these syndromes are also associated with common aetiologies and prognosis.

When seeing a child presenting after a seizure, important questions to ask include:

- Was it really a seizure?
  If so,
- What sort of seizure was it?
- What is the cause of the epilepsy?
- What is the epilepsy syndrome?

Was it really a seizure?

Several other conditions can be mistaken for epileptic seizures (Table 1). Taking careful histories from the child and an eye witness are crucial to

IN SUMMARY

- **Epilepsy is a group of disorders associated with recurrent unprovoked seizures.**
- **An EEG is recommended following a first afebrile single seizure but imaging is not required in all children with epilepsy.**
- **Anticonvulsant medications are usually commenced after two or more unprovoked afebrile seizures. Sodium valproate is recommended for generalised epilepsy and carbamazepine or sodium valproate for focal epilepsy.**
- **Childhood epilepsy generally has a good prognosis, with around two-thirds of patients responding to treatment and more than half ultimately 'outgrowing' their epilepsy.**
- **Surgery offers the best chance of cure in the 20 to 30% of children who have medically refractory epilepsy.**

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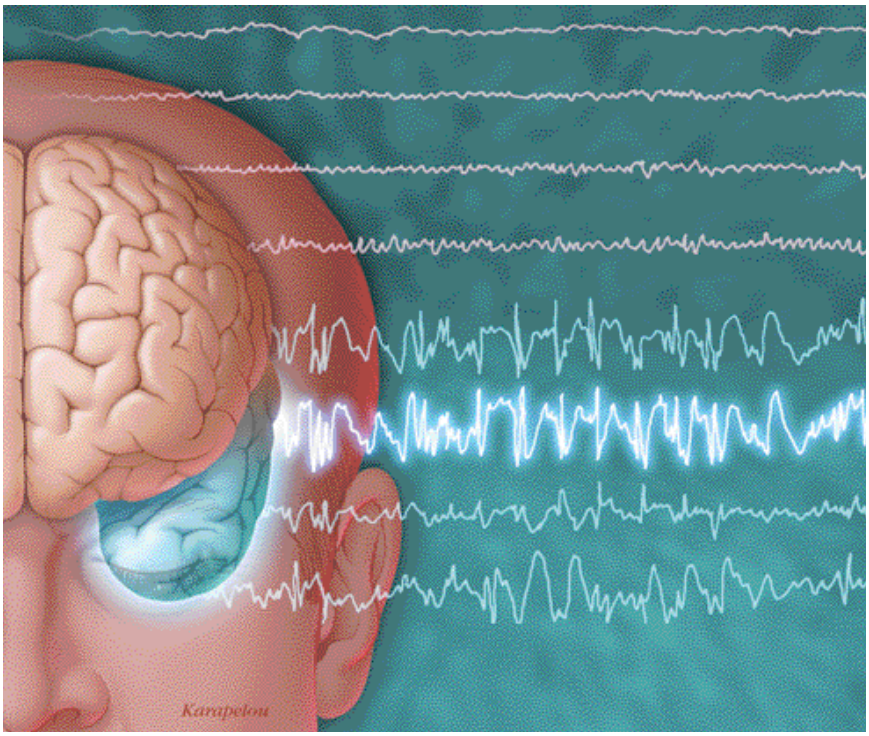

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making a correct diagnosis. Syncope is the most common condition that is confused with seizures because it is often associated with convulsive movements.

Table 1. Differential diagnoses of epileptic seizures

Tonic, clonic and tonic–clonic seizures
- Convulsive syncope
- Breath-holding spells
- Psychogenic seizures

Absence and complex partial seizures
- Day dreaming
- Psychogenic unresponsiveness

Myoclonic seizures
- Sleep myoclonus
- Tics
- Infantile shuddering attacks
- Startle response

The circumstances leading up to the event are important. Were there precipitants such as pain or fear to suggest a vasovagal episode, or was the child standing or sitting for a prolonged period to suggest postural hypotension? In infants and preschoolers, breath-holding spells provoked by trivial injury can sometimes be mistaken for seizures. Breath-holding is probably genetically predetermined, and it can be associated with iron deficiency. Other disorders mistaken for seizures include tics and sleep myoclonus.

What sort of seizure was it?

Febrile and afebrile seizures

It is important to differentiate between febrile and afebrile seizures in preschool children. Febrile seizures affect approximately 3% of children between the ages of 3 months and 5 years, with the peak incidence in the second year of life. One-third of the affected children will have recurrent episodes, and around 3% of these children will later develop epilepsy. Children with febrile convulsions do not require treatment with anticonvulsants except in the rare cases of recurrent prolonged bouts of febrile status epilepticus. There is no evidence that anticonvulsants alter the natural history of febrile convulsions or reduce the risk of the child later developing epilepsy.

Focal and generalised seizures

The International League against Epilepsy (ILAE) classification divides seizures into two broad categories, focal and generalised (Table 2).[4] Generalised seizures are associated with initial activation of neurones in both hemispheres, and focal seizures are associated with initial activation of a limited number of neurones in part of one hemisphere. Focal seizures are further divided into simple focal or complex focal, depending on whether consciousness is preserved (consciousness is preserved in simple focal seizures). However, this division is often difficult to determine in young children.

Symptomatology in focal seizures depends on the site of origin and spread patterns. For example, seizures arising from the primary motor strip in the posterior frontal lobe are associated with focal clonic jerking. This may spread in a 'Jacksonian march' to adjacent areas of motor cortex. In contrast, seizures arising from more anteriorly within the frontal lobe or from the temporal lobe are associated with oral and motor automatisms. (Automatisms are seemingly purposeful involuntary movements during a state of altered consciousness.) Seizures arising from the occipital lobe can be associated with visual symptoms such as flashing lights or more complex formed hallucinations.

Focal seizures not uncommonly secondarily generalise, giving the false impression of a primary generalised seizure, particularly in children with nocturnal seizures when the onset is not witnessed by parents.

What is the cause of the epilepsy?

Idiopathic and generalised epilepsies

The term idiopathic is used for epilepsies with presumed genetic aetiology. Idiopathic epilepsies usually occur in children with normal development and physical examination. They generally have a predictable age of onset and a good prognosis with regard to later seizure remission.

In contrast, the term symptomatic refers to epilepsies caused by underlying brain abnormalities. Cortical malformations are the most commonly identified pathological substrate for symptomatic childhood epilepsy, particularly in children with intractable and surgically-treatable epilepsy, where they account for up to 40% of cases.[5] Cortical malformations are nonprogressive lesions that occur early in brain development; they are being more frequently recognised now that magnetic resonance imaging (MRI) has become more widely available (Figure 1). Other causes of symptomatic epilepsy include developmental tumours and metabolic or genetic disorders such as tuberous sclerosis.

What is the epilepsy syndrome?

Accurate characterisation of the epilepsy syndrome determines the choice of treatment and influences prognosis. Epilepsy can be divided into four categories based on seizure type and aetiology:[6]

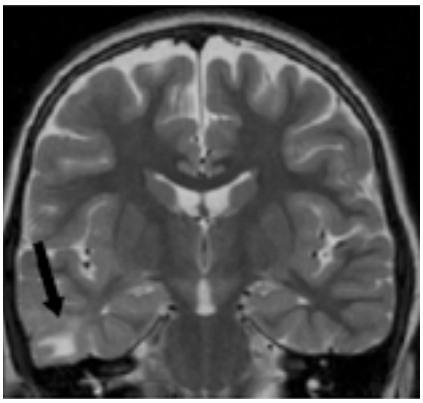

Figure 1. Symptomatic epilepsy. MRI showing right temporal lobe focal cortical dysplasia in a child with refractory complex focal seizures.

- idiopathic generalised
- idiopathic focal
- symptomatic generalised
- symptomatic focal.

The common childhood and adolescent epilepsy syndromes are discussed below, as are the less common forms that it is important not to miss (Table 3).[7]

Table 2. Classification of seizures[4]

Generalised seizures

Tonic–clonic
Clonic
Tonic
Absence
Myoclonic
Atonic (astatic)
Epileptic spasms

Focal seizures

Focal motor:

- Clonic
- Asymmetrical tonic
- With automatisms
- Hyperkinetic

Hemiclonic
Secondarily generalised
Sensory:

- Elementary
- Experiential

Common childhood epilepsy syndromes

Childhood absence epilepsy

Childhood absence epilepsy (CAE), also known as petit mal epilepsy, is the most common idiopathic generalised epilepsy syndrome, accounting for 2 to 8% of all cases. It typically affects primary school age children, and 30% of cases have a positive family history. The seizures are associated with brief episodes of unresponsiveness and behavioural arrest lasting less than 30 seconds, multiple times per day. The EEG shows bisynchronous 3 Hz spike wave (Figure 2). It is the

Table 3. Important childhood and adolescent epilepsy syndromes

Epilepsy syndrome	Syndrome type	Seizure type
Childhood absence epilepsy (petit mal epilepsy)	Idiopathic generalised	Absence
Benign epilepsy with centrotemporal spikes (benign rolandic epilepsy)	Idiopathic focal	Simple focal, may become secondarily generalised
Juvenile myoclonic epilepsy	Idiopathic generalised	Myoclonic, tonic–clonic, absence
Temporal lobe epilepsy	Symptomatic focal	Simple focal or complex focal
West syndrome (infantile spasms)	Symptomatic generalised	Tonic
Lennox–Gastaut	Symptomatic generalised	Tonic, and others

only form of epilepsy that can be easily diagnosed in the consulting room as it can be induced by asking the child to perform hyperventilation.

Sodium valproate (Epilim, Valpro) is the treatment of first choice, and seizure remission is achieved in 80 to 90% of children. However, it is important to note that up to 40% of cases can later develop generalised tonic–clonic seizures during adolescence.

Benign epilepsy with centrotemporal spikes

Benign epilepsy with centrotemporal spikes (BECTS), also known as benign rolandic epilepsy, is the most common idiopathic focal epilepsy syndrome. The peak age of onset is at 7 to 9 years of age, and it accounts for 15% of all cases. The simple focal seizures usually occur during sleep. They can be associated with facial twitching, tingling, drooling or inability to speak, and they frequently secondarily generalise. The EEG shows a characteristic pattern of unilateral or independent bilateral epileptic discharges over the low posterior frontal ('central') region with activation during sleep (Figure 3).

BECTS responds well to treatment with sodium valproate or carbamazepine (Tegretol, Teril). It has an excellent prognosis with almost universal seizure remission by puberty.

Juvenile myoclonic epilepsy

Juvenile myoclonic epilepsy (JME) is a form of idiopathic generalised epilepsy and accounts for 5 to 10% of all cases. It typically presents between 12 and 18 years of age. This condition has a strong genetic predisposition. Early morning myoclonus is the hallmark feature, triggered by fatigue, sleep deprivation and alcohol. It often goes unrecognised and patients may only be diagnosed with JME following their first generalised tonic clonic seizure. The EEG characteristically shows generalised bursts of fast (>3 Hz) polyspike wave discharges (Figure 4).

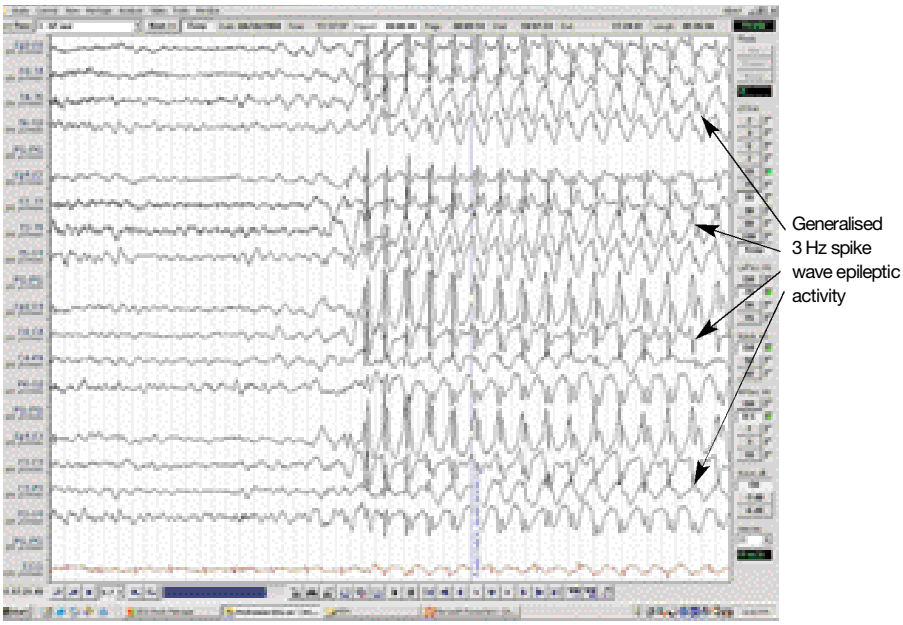

Figure 2. Childhood absence epilepsy. EEG showing an absence seizure associated with 3 Hz generalised spike wave activity in a 6-year-old child.

JME usually has an excellent response to sodium valproate. However, it is a life long condition, seizures usually recurring within weeks or months if medication is ceased. Most neurologists, therefore, recommend patients remain on anticonvulsants indefinitely.

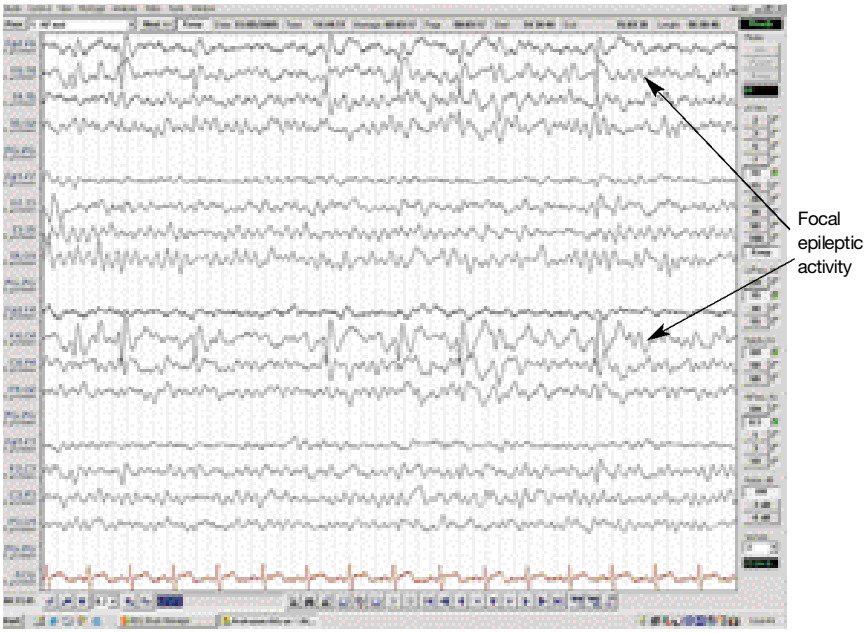

Figure 3. Benign epilepsy with centrotemporal spikes. EEG showing focal centrotemporal spike wave discharges over the right hemisphere in an 8-year-old child.

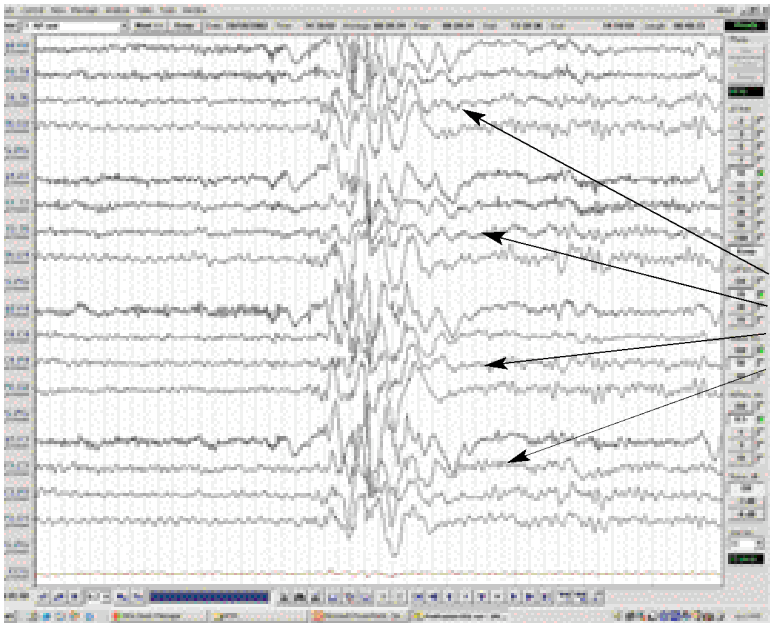

Figure 4. Juvenile myoclonic epilepsy. EEG showing generalised polyspike wave epileptic discharges in a 14-year-old boy.

Less common but important childhood epilepsies

Temporal lobe epilepsy

Temporal lobe epilepsy (TLE) is a form of symptomatic focal epilepsy, caused by pathology including hippocampal sclerosis (Figure 5), developmental tumours and cortical malformations. Seizures can be simple focal or complex focal. The EEG shows unilateral or bilateral temporal slowing or focal spike discharges, activated during sleep. TLE is often refractory to medications, and it is the most frequent reason for epilepsy surgery in adults.[8]

West syndrome

West syndrome or infantile spasms refers to the triad of epileptic spasms, EEG pattern of hypsarrhythmia (electrical chaos) and developmental arrest. The syndrome has a peak age of onset between 3 and 7 months, with almost all cases presenting before 2 years of age. More than two-thirds of cases are symptomatic, usually due to structural CNS abnormalities. The infantile spasms can be flexor, extensor or mixed, and typically occur in clusters 5 to 30 seconds apart, often on waking.

Corticosteroids and vigabatrin (Sabril) are the most effective treatments.[9]

Lennox–Gastaut syndrome

Some children with West syndrome may respond to treatment but many go on to develop Lennox–Gastaut syndrome (LGS), a form of symptomatic generalised epilepsy. LGS accounts for 2 to 3% of all epilepsies, and has its peak age of onset between 3 and 5 years. It is associated with multiple seizures types; particularly axial tonic seizures causing injury, but atypical absence, atonic, tonic–clonic and myoclonic seizures are also common. The EEG characteristically shows generalised slow (<3 Hz) spike wave activity, and background rhythms are poorly developed for age. Mental retardation, behavioural problems and recurrent bouts of status epilepticus are common.

LGS responds poorly to treatment but combinations of sodium valproate and lamotrigine (Elmendos, Lamictal, Lamitrin, Lamogine, Seaze) or topiramate (Topamax) appear to be the best anticonvulsants.

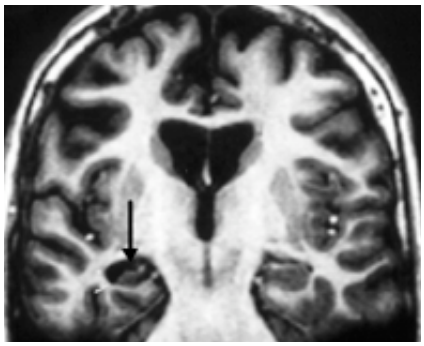

Figure 5. Temporal lobe epilepsy (a form of symptomatic focal epilepsy). MRI of the brain showing atrophy of the right hippocampus with dilation of the overlying temporal horn of the right lateral ventricle.

Investigations

It is reasonable to measure serum electrolytes, calcium, magnesium and glucose after a first seizure, but abnormalities are rarely identified except in infants less than six months of age. An EEG is usually indicated after a first seizure; it is important in confirming the clinical diagnosis and enabling differentiation between focal and generalised seizures. Activation procedures such as hyperventilation and photic stimulation increase the diagnostic yield in patients who have generalised epilepsy.

EEG

An abnormal EEG is predictive of seizure recurrence. An evidence based review showed that 54% of patients with abnormal EEGs had further seizures, compared to 25% of those with normal EEGs ($p<0.001$).[10]

The EEG also helps to accurately characterise the specific epilepsy syndrome. This influences choice of medications and provides information about the long term prognosis.

MRI

MRI is the imaging modality of choice in children with epilepsy. It is not required in all cases but should be performed in children with focal seizures (other than

benign epilepsy with centrotemporal spikes) or focal EEG abnormalities and in children with associated neurological problems such as motor impairment or intellectual disability.

Treatment

General principles of treatment include avoidance of precipitating factors such as sleep deprivation. Parents should be counselled about taking safety precautions, particularly supervising their children when bathing or swimming. Seizures rarely last more than three minutes in most children, and parents should be reassured that short seizures do not cause brain damage. They should be instructed in the first aid treatment of generalised seizures. Emergency treatments such as rectal diazepam (Antenex, Ducene, Valium, Valpam) or buccal midazolam (Hypnovel) should be discussed for children with a history of prolonged seizures (see later under 'Emergency treatment').

For most types of epilepsy, maintenance anticonvulsants are generally recommended after two unprovoked seizures.

Maintenance anticonvulsant therapy

There are many anticonvulsants available to treat epilepsy but the choice of drug needs to take into account various factors, including the age of the child and the specific epilepsy syndrome. Sodium valproate and carbamazepine are the most commonly prescribed medications.

Generalised epilepsies

Sodium valproate is the initial treatment of choice for the generalised epilepsies. Potential side effects include nausea, vomiting, increased appetite resulting in weight gain, thrombocytopenia, leucopenia, tremor and thinning of the hair. Caution needs to be exercised in children less than 2 years of age, particularly in those with developmental delay or those on other anticonvulsants, because of the one in 800 risk of idiosyncratic hepatic failure.

Other drugs effective against generalised epilepsies include the benzodiazepines clonazepam (Paxam, Rivotril) and clobazam (Frisium), and lamotrigine and topiramate. Ethosuximide (Zarontin) is only effective in absence epilepsy.

Focal epilepsies

Carbamazepine is the initial treatment of choice for the focal epilepsies but sodium valproate has also been shown to be effective. Side effects include leucopenia, liver function abnormalities, hyponatraemia, allergic rashes (in 3 to 5% of patients) and, rarely, Stevens–Johnson syndrome. Drugs that inhibit the hepatic cytochrome P450 enzyme system (such as erythromycin) should be avoided because they can result in carbamazepine toxicity. It is also important to remember that carbamazepine can exacerbate some forms of primary generalised epilepsy, particularly in children with absence and myoclonic seizures.

All the newer anticonvulsants are effective against focal seizures. These include lamotrigine, topiramate, gabapentin, tiagabine (Gabitril), oxcarbazepine (Trileptal), levetiracetam (Keppra) and pregabalin (Lyrica). Several have been recently compared in an evidence based review.[11]

Prognosis and weaning of anticonvulsants

Most children with epilepsy respond well to medications, with more than 60% of patients achieving two-year remission. Syndromes such as BECTS and CAE have an excellent response to therapy. However, the presence of an underlying structural brain lesion, persistent seizures two years after starting treatment and a persistently abnormal EEG are predictive of poor response.

Once a child enters seizure remission, the decision to wean medications should take into account factors such as the natural history of the epilepsy syndrome and the likelihood of relapse. The long term prognosis following discontinuation of treatment is generally quite good. For example, 60 to 75% of children who are controlled for more than four years will remain seizure free after medications are withdrawn.[12]

Discontinuing medications is reasonable after two years in the idiopathic epilepsies like BECTS and CAE. More prolonged treatment is appropriate in the symptomatic epilepsies. As a general principle, medications should be weaned slowly, particularly the barbiturates and benzodiazepines because withdrawal seizures are more likely with these. Most patients who relapse do so within three months.[13] Predictors of relapse include symptomatic epilepsy, the severity of the epilepsy and the presence of associated mental retardation or neurological deficits.

Serum anticonvulsant levels and monitoring for side effects

Dosage changes should be based on clinical response rather than on serum anticonvulsant levels. Monitoring of serum anticonvulsant levels is only useful for those drugs where serum levels have a reasonable correlation with clinical signs of toxicity. This applies to phenytoin because of saturable kinetics, and to a lesser extent carbamazepine and phenobarbitone. Serum drug levels are also useful when there is a poor response at an adequate dose or when noncompliance is suspected.

Similarly, routine screening for the side effects of anticonvulsant therapy is of questionable value in asymptomatic patients. Such screening does not predict severe idiosyncratic skin eruptions such as Stevens–Johnson syndrome and other hypersensitivity reactions.

Other treatments options

About 20 to 30% of children have medically refractory epilepsy. The likelihood of achieving seizure remission falls

Useful web based resources

For clinicians

Royal Children's Hospital, Melbourne, Children's Epilepsy Program
www.rch.org.au/cep

American Epilepsy Society
www.aesnet.org

American Academy of Neurology
www.aan.com

For patients and families

Children's Epilepsy Program
www.rch.org.au/cep

Epilepsy Australia (the National Coalition of Epilepsy Associations)
www.epilepsyaustralia.org

Epilepsy Action Australia
www.epilepsy.org.au

dramatically after failure to respond to two anticonvulsants. Surgery offers the best hope of cure for these patients. Outcomes of surgery vary, depending on the epilepsy syndrome, but 40 to 70% of appropriately selected patients will become seizure-free.[14]

Other treatment options include the ketogenic diet, brain stimulation and immunotherapies.

Emergency treatment of prolonged seizures

Epilepsy seizures usually terminate within two to three minutes and there is a refractory period in many patients lasting minutes to hours before another seizure can occur. Status epilepticus (convulsive seizures lasting longer than 30 minutes) is due to persistence of excitatory or failure of inhibitory mechanisms.

Prehospital treatment of prolonged seizures with rectal diazepam (0.3 to 0.5 mg diazepam per kg bodyweight to a maximum of 10 mg) or intransal/buccal midazolam (0.1 mg midazolam per kg bodyweight to a maximum of 10 mg) is safe and effective.[15] Respiratory depression is rarely seen.

Conclusion

Epilepsy is a common childhood condition. Diagnosis is primarily based on the clinical history but an EEG is important in confirming the diagnosis and helping to differentiate between focal and generalised seizures. Most children respond to anticonvulsant mediation. Prognosis is influenced by the epilepsy syndrome but about half of children will have long term remission of seizures.

More information is available from the web based resources listed in the box on this page. MT

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DECLARATION OF INTEREST: Dr Mackay has given lectures on behalf of GlaxoSmithKline Australia, Janssen-Cilag and Sanofi-Aventis.

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