

APPROACH TO EPILEPSY IN CHILDHOOD

A small rural epidemiological study in the Northern Province described a prevalence of epilepsy of 6.7 per 1 000 South African children.¹ For the whole of Africa the figure ranges between 2.9 and 26 per 1 000 children.^{1,2}



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Between 2000 and 2002, 1 087 children attended the epilepsy clinic at Red Cross Children's Hospital, accounting for over 60% of patients attending the paediatric neurology clinics. Of these children, 45% had an underlying cause for their epilepsy (symptomatic), while the remainder were cryptogenic or idiopathic. In the symptomatic group the condition was potentially preventable in 63% and included hypoxic ischaemic encephalitis, meningitis, tuberculomas, neurocysticercosis and trauma. Of the total group 15% had 'intractable forms of epilepsy' and 59% had a level of neurodisability which required the child to be placed in a day care facility, training centre or to receive special needs education. Similar results are found in other developing countries.^{3,4} However, at Red Cross Children's Hospital we are seeing only the 'tip of the iceberg' as many children are managed at primary and secondary level. At least 50% children with epilepsy in developing countries are not treated, owing to a combination of lack of access to medical resources and the continuing stigma around epilepsy.^{1,3}

When does a child have epilepsy?

Any neurologically stressed individual can have a seizure, but this does not necessarily mean s/he has epilepsy. A convulsion can occur as part of an intercurrent illness, transient hypoxia or biochemical imbalance. Unless brain injury occurs epilepsy is unlikely to develop. Only in exceptional circumstances is a child labelled epileptic after the first seizure (e.g. infantile spasm).

If there are 2 or more eye-witness descriptions of isolated seizure events then epilepsy should be diagnosed, once acute reversible causes are excluded such as electrolyte imbalance, hypoxia or infections. The attending physician should try and define the type of epilepsy as early as possible. It is important to realise that there are many other events that may be misdiagnosed as epilepsy, but are in fact paroxysms (Table I).

What is the role of the general practitioner?

Epilepsy is a common disorder, and without primary level input and co-ordination, the secondary and tertiary services will not cope. Non-complex epilepsy (e.g. absence, benign focal epilepsy of childhood) can be managed mainly by a GP once a paediatrician has established the diagnosis and recommended treatment. Complex epilepsies (e.g. infantile spasms, Lennox-Gastaut syndrome, severe myoclonic epilepsy of infancy (SMEI)) need to be managed in collaboration with the paediatrician and paediatric neurology services.

When to perform an EEG

An EEG should be requested after 2 or more seizures. It is helpful to request an EEG either before or on the day of referral to the specialist. To gain maximum information from the EEG, request an awake study with hyperventilation for sus-

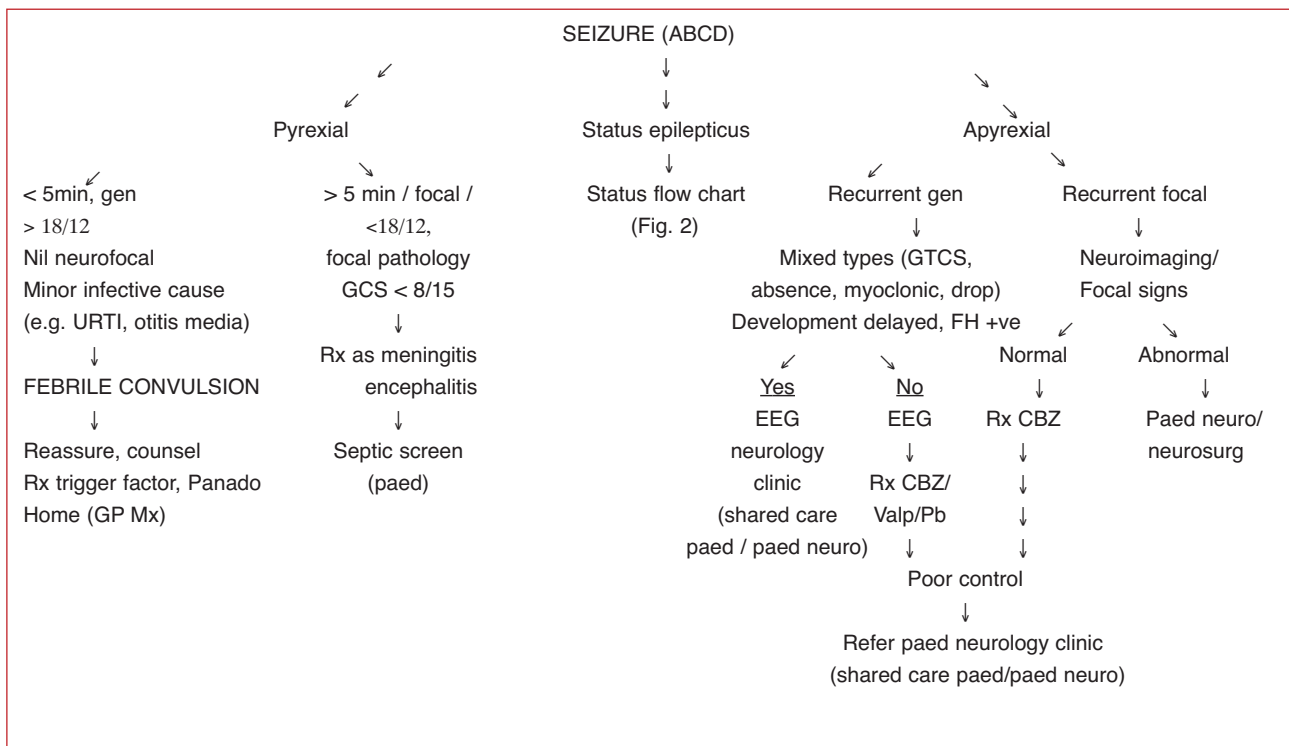


Fig. 1. Epilepsy flow chart (A = airway; B = breathing; C = cardiac; D = dextrostix / neurodisability; GCS = Glasgow coma score; GTCS = generalised tonic-clonic seizures; CBZ = carbamazepine; Valp = sodium valproate; Pb = phenobarbitone; FH + ve = Family history positive)

pected absence epilepsy and a sleep study (sleep-deprive the child) for suspected complex partial epilepsy. Infantile spasms are a medical emergency and an EEG must be performed within 24 hours with no delay in starting treatment.

Typical febrile convulsions do not need an EEG, but a child with atypical features may have generalised epilepsy with febrile seizures (GEFS +), or SMEI and an EEG may be useful. An EEG is performed over a relatively short period (usually 30 minutes), and a normal study does not automatically exclude epilepsy. If the history and/or clinical picture is consistent with a seizure disorder then the child should be managed as such.

When to perform neuroimaging

Whenever there are focal features to the seizure, neuroimaging is recommended to exclude a space-occupying lesion, cerebral malformation or infective focus. Computed tomography (CT) scanning is usually sufficient.

Other investigations

Exclude meningitis through CSF analysis in any infant below 18 months of age with a febrile convulsion, and consider it in any other child who is pyrexial. Avoid lumbar puncture if there is any evidence of raised intracranial pressure or focal pathology. In these cases perform neuroimaging first. Acute seizures always warrant a blood glucose and acid-base analysis. Metabolic screens are occasionally needed but should be co-ordinated through a tertiary centre. Unusual features in the history or clinical presentation suggest toxicology.

Neonatal seizures

Neonatal seizures are common and often very subtle. The majority are related to hypoxic ischaemic encephalopathy (HIE), intracranial haemorrhage, intracranial infection and developmental anomalies. It is essential to exclude treatable causes. These are biochemical dysfunction, infection and intraventricular or cerebral haemorrhage. First-line therapy is phenobarbitone. Sodium valproate,

carbamazepine and the benzodiazepines are used in resistant cases. Metabolic disorders are rare, but should be considered once common causes are excluded, especially with a history of consanguinity or family history of neonatal seizures. Biotinidase deficiency and pyridoxine dependency are dramatically responsive to replacement therapy.

Fig. 1 gives a summary of a simple approach to the child presenting acutely with convulsions.

Febrile convulsions

Febrile convulsions are seen in a child with a pyrexial illness, with a clear focus of infection, who has a generalised convulsion for less than 5 minutes. The child should be more than 18 months old and clinically stable with no focal neurology. Management consists of reassurance, temperature control and advice that the child may have more seizures but will eventually 'grow out of it'. Lumbar puncture must be performed in all children below 18 months of age, and a CT scan must be performed if there are focal features.

Atypical febrile convulsions which persist beyond 6 years of age are found in a group of children, and have been labelled GEFS +.⁵ The syndrome ranges in severity from simple recurrent febrile convulsions which eventually resolve after 6 years of age, to a severe seizure disorder with additional events of afebrile generalised seizures, myoclonic and drop attacks. Several gene loci for this condition have been identified and SMEI is the worst end of the spectrum.

TYPES OF EPILEPSY

The International League Against Epilepsy (ILAE) has devised systems for categorising epilepsy.⁶ This falls into 3 main groups — focal, generalised and syndromic, further subdivided into symptomatic, idiopathic and cryptogenic. This categorisation of epilepsy allows more directional treatment and consequently better long-term prog-

noses. This article will cover only the commoner forms and those which have the most impact (see also Tables I - III for details of each type).

Focal epilepsy (Table II)

The focal epilepsies are the predominant group of epilepsies in children over 6 years of age.⁷ In simple partial seizures consciousness is preserved, with loss of consciousness during complex partial seizures. Episodes last 30 seconds to a few minutes. The child may continue to walk or even talk but appears unfocused. Automatisms (repetitive, purposeless mannerisms) are common.

Temporal lobe epilepsy can be very resistant to medical therapy, especially if associated with mesial temporal sclerosis, with or without a history of prolonged febrile convulsions. This form of epilepsy can be debilitating and progress into adulthood. It is

increasingly managed surgically.

The commonest symptomatic focal epilepsies in South Africa are due to neurocysticercosis and tuberculosis granulomas. In most patients seizures are isolated and do not require treatment. For recurrent seizures, carbamazepine is the first-line agent in secondary and tertiary facilities. However phenobarbitone may be used in the child from an isolated region without easy access to medical facilities.

Generalised epilepsy (Table III)

Children between 1 and 6 years are more likely to have a generalised form of epilepsy.⁷ Generalised tonic clonic seizures in children below 1 year of age are rare. There is an association with various metabolic and neurodegenerative conditions, so early referral should be considered, especially if there is any evidence of neuroregression. Treatment is with either sodium valproate or carbamazepine.

Table I. **Paroxysmal events**

Reflex anoxic attacks ('breath-holding attacks') — shared care GP/paediatrician

- Common
- Toddler to 6-year-old age group
- Vagally mediated, usually triggered by crying or pain
- The child takes a deep gasp, stops breathing, becomes pale or blue with brief loss of consciousness
- Spontaneously recovers and no neurological sequelae are evident
- Management: reassurance (difficult to give unless the parent has experienced a series of episodes and knows the child always fully recovers)
- Differential diagnoses: sepsis, seizures, metabolic conditions, cardiac arrhythmias and Munchausen's syndrome by proxy
- Events are exacerbated by iron deficiency anaemia and a trial of iron therapy should be considered

Syncope (fainting) — shared care GP/paediatrician

- Common in adolescent girls but can affect all age groups
- Vagally mediated
- Attacks can be very abrupt and easily confused with seizures
- Exclude long QT interval

Benign paroxysmal vertigo — shared care GP/paediatrician

- Toddlers
- Appear pale and frightened, run to a carer and cling to them and may vomit
- Last no more than a few minutes and the child appears completely well afterwards
- Differential diagnosis is temporal lobe epilepsy (request a sleep EEG)

Pseudoseizures — shared care GP/paediatrician

- A diagnosis of exclusion
- Commonest in adolescent girls
- Dramatic with rolling on the ground, random flinging about of limbs with eyes closed
- Incontinence can occur
- Children with confirmed epilepsy also can have pseudoseizures
- Events may represent a response to abuse (often sexual)

Table II. **Focal epilepsies****Benign focal epilepsy of childhood (BFEC, Rolandic epilepsy) — shared care GP/paediatrician**

- Commonest form of childhood focal epilepsy
- Onset is typically between 8 and 12 years of age
- Onset is often from sleep and the child has focal motor facial twitching which rarely has secondary generalisation
- The child is usually aware during the event but cannot talk until the seizure terminates
- Events are usually short and infrequent
- Not all patients require therapy; those that do have a good response to carbamazepine
- Seizures resolve after adolescence

Benign epilepsy with occipital paroxysms (BEOP) — shared care GP/paediatrician

- The second commonest form of childhood focal epilepsy
- Events are very infrequent, typically from sleep and can be prolonged
- Often visual manifestations or temporary blindness, intense headache and vomiting occur during the event
- The EEG shows typical occipital paroxysms
- Therapy is not always necessary and the natural history is for spontaneous resolution

Table III. **Generalised epilepsies****Childhood absence epilepsy (CAE) — shared care GP/paediatrician**

- Commonest form
- Onset 4 - 6 years
- Brief episodes of unresponsiveness (no more than 10 seconds) and gross motor arrest
- May be simple automatisms and resolution typically by adolescence

Juvenile myoclonic epilepsy (JME) — shared care GP/paediatrician

- Commonest adolescent form of epilepsy
- Onset between 8 and 14 years
- Often photosensitivity and check for myoclonus on awakening

Atypical absences — shared care paediatrician/paed neurologist

- Prolonged with atypical EEG features
- Associated with various epilepsy syndromes
- Poorer cognitive outcome
- Medication is with sodium valproate as first line after exclusion of a metabolic condition

Tonic seizures — shared care paediatrician/paed neurologist

- Occurs in isolation or as part of epilepsy syndromes
- Difficult seizures to control
- May be associated with serious autonomic dysfunction
- First-line treatment is with carbamazepine

Myoclonic seizures — shared care paediatrician/paed neurologist

- Short (microseconds) of muscular contraction, typically involving the arms, head and trunk
- Events range from a head nod to being thrown across the room
- These children often need helmets
- Referral to a specialised neurology unit is warranted, especially if there is neuroregression and/or ataxia

Drop attacks — shared care paediatrician/paed neurologist

- Usually associated with epilepsy syndromes
- Tonic (stiff fall) or atonic (droop fall/slump)
- Episodes are short and not associated with post-ictal drowsiness
- Child appears surprised, picks himself up and continues his activities
- Rarely benign and these children should be referred to a neurologist

Table IV. **Epilepsy syndromes****Infantile spasms — shared care paediatrician/paed neurologist**

- True neurological emergencies
- Onset between 3 and 6 months
- Often misdiagnosed as colic
- Infant has runs of head and trunk flexion and arms and legs 'flinging out' with the contraction held for 1 - 2 seconds
- The episode distresses the baby, there is usually a cry
- These children are undergoing a degenerative neuroencephalopathic process (West syndrome)
- Delay in gaining seizure control will be reflected in the severity of the outcome
- Immediate admission with EEG performed the same day (to confirm hypsarrhythmia and burst suppression)
- Management: Steroids (ACTH) in South Africa; alternative — vigabatrin. Long-term management usually with sodium valproate and a benzodiazepine
- Neurometabolic investigations and neuroimaging to exclude tuberous sclerosis unless a clear underlying aetiology is evident, e.g. history of birth asphyxia

Severe myoclonic epilepsy of infancy — shared care paediatrician/paed neurologist

- Onset < 1 year of age
- Clusters of atypical febrile convulsion
- Later afebrile generalised tonic-clonic and myoclonic events
- Neuroregression often follows by 2 years of age

Lennox-Gastaut syndrome — shared care paediatrician/paed neurologist

- Can occur independently or follow on from infantile spasms (West syndrome)
- Onset from 2 years of age
- Combination of drop attacks, myoclonic seizures and occasional generalised tonic-clonic seizures

Landau-Kleffner syndrome — shared care paediatrician/paed neurologist

- Presents around 2 years of age in a previously normal child
- In a child with normal hearing who has lost expressive and receptive language over a few days to weeks consider LKS and perform a sleep EEG
- Diagnosis of this rare condition requires early specialist intervention

The differentiation between complex partial seizures and absence epilepsy is important. The former is treated with carbamazepine, and the latter with sodium valproate. Treating a child who has absence epilepsy with carbamazepine may cause absence status.

Epilepsy syndromes (Table IV)

Many epilepsy syndromes are now recognised; however, infantile spasms, severe myoclonic epilepsy of infancy, Lennox-Gastaut syndrome and Landau-Kleffner syndrome (LKS) are the most relevant, since they have major neuro-cognitive impact.

Status epilepticus

This is defined as a generalised convulsion that lasts 30 minutes or more. It can occur as continuous seizure activity or the child may go in and out of ictus, with the concomitant risk of sustained brain damage. Management is summarised in Fig. 2. The following

alternatives can be considered:

- Lorazepam (0.1 mg/kg) is a faster acting alternative to diazepam for bolus IV intervention.
- Midazolam intranasally (200 µg/kg) or sublingually (500 µg/kg) if there is no venous access.

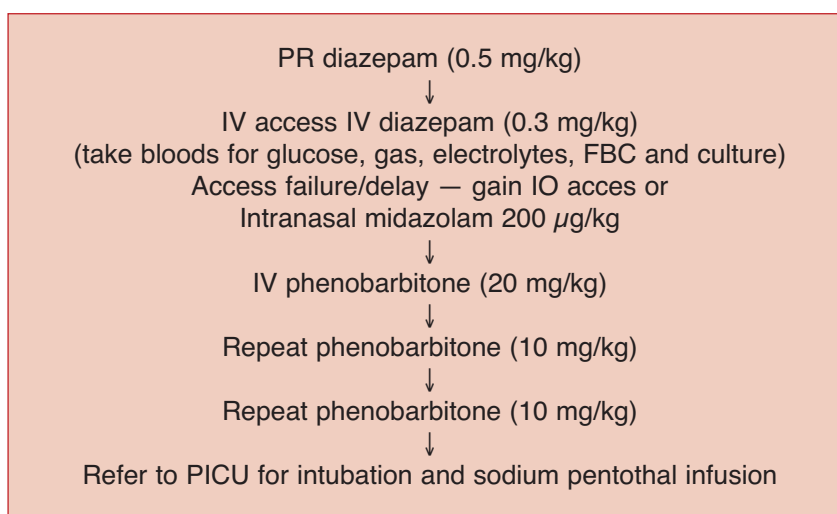


Fig. 2. Management of status epilepticus. ABCD (oxygen, monitor saturation, pulse and blood pressure, glucose). (PR = per rectum; FBC = full blood count; IO = intraosseous; PICU = paediatric intensive care unit.)

Epilepsy is a common disorder, and without primary level input and co-ordination, the secondary and tertiary services will not cope.

If there are 2 or more eyewitness descriptions of isolated seizure events then epilepsy should be diagnosed, once acute reversible causes are excluded such as electrolyte imbalance, hypoxia or infections.

- Midazolam infusion loading at 200 µg/kg by slow IV injection, then titrating an infusion between 30 - 300 µg/kg/h. Alternatively, clonazepam (Rivotril) infusion if seizure control is not gained after the first phenobarbitone infusion.
- Phenytoin (20 mg/kg over 20 minutes) if there is a known adverse reaction to phenobarbitone (monitor for cardiac arrhythmias).

Watch carefully for drug-related respiratory depression. Intubation, ventilation and administration of sodium pentothal infusion should only be performed in a centre with trained anaesthetic and paediatric intensive care.

TREATMENT

Routine medication

Phenobarbitone is the cheapest and most readily available agent in South Africa for routine treatment of epilepsy and for non-complex seizure disorders in children who are not based near a tertiary or secondary centre it is better to use this than nothing at all. There is also a place for phenobarbitone in children with profound brain damage, such as those with cerebral palsy with static encephalopathy. A daily dose of phenobarbitone given to a medically resistant child can make all the difference to quality of life. For older children phenobarbitone is associated with hyperactivity, poor concentration and behavioural problems. Parents

must be warned of this and asked to report these features early.⁸

Agents routinely used internationally and increasingly in South Africa, are sodium valproate and carbamazepine. Traditionally generalised seizure disorders are treated with sodium valproate, while partial epilepsies are treated with carbamazepine. Carbamazepine exacerbates absence and myoclonic forms of epilepsy. Sodium valproate should be used with caution in children under 1 year and in those with suspected metabolic disorders. Drug levels are unhelpful unless there is suspected toxicity or lack of compliance. Ethosuximide is used mainly for patients with absence epilepsy resistant to, or intolerant of, valproate.

The benzodiazepines have roles in both acute and chronic epilepsy. Diazepam is used routinely in status epilepticus. Alternatives are midazolam, which can be used intranasally and sublingually, and lorazepam. Clonazepam or clobazam are used long-term, and are both very good for myoclonic and drop attacks. Tolerance tends to develop after 3 months and drug 'holidays' are helpful.

Second-line agents are lamotrigine, topiramate, gabapentin and vigabatrin.⁹ Lamotrigine has had a major impact on children with resistant seizure disorders — especially those with Lennox-Gastaut syndrome. It is expensive and only available to children with access to tertiary centres. Topiramate is described particularly for partial epilepsies and more recently for infantile spasms. It can cause dramatic loss of appetite and must be dose-titrated carefully. Vigabatrin is an effective agent for structural lesions and infantile spasms but has lost favour since visual field defects were described. It also has serious effects on behaviour. Other new agents on the market include levetiracetam, which may be very effective in photosensitive forms of epilepsy.

Alternative therapies include trials of biotin, pyridoxine and folate, most

effective in the neonatal and infancy period, but there are cases of pyridoxine-responsive epilepsies in older children. Acetazolamide has a role in resistant epilepsies. Steroids can be used as a 6-week course and there is anecdotal evidence for weekly treatment in some forms of epilepsy (continuous spike wave in sleep (CSWS), LKS).

How long to treat for

Generally a 2-year seizure-free period is recommended before trying gently to wean off medication. Shorter courses are acceptable for tuberculomas and neurocysticercosis where disease activity is limited. Similarly children who required prophylaxis during acute admission, e.g. seizures as part of a head injury or meningitis, often have resolution of epileptogenic activity within 3 months unless a brain lesion persists. Parents should be warned that some forms of epilepsy do not remit, such as juvenile myoclonic epilepsy and Lennox-Gastaut syndrome.

Intractable epilepsy

Intractable epilepsy describes persistent seizures despite the use of 2 or more agents. In reality it is often not the seizures that are debilitating, but the impact they have on the child and the family. The problems of sleepless nights, post-ictal drowsiness and irritation, poor concentration in class, drowsiness and other side-effects from the drugs, and lack of independence in adolescence with over-protection from parents, have often driven practitioners to look at alternative treatments.

Alternatives to medication

Complex patients with intractable epilepsy should be managed within the paediatric neurology service where they can have an 'epilepsy work-up'. This includes a combination of video EEG telemetry, neuroimaging and metabolic investigations to define the epilepsy semiology. From these data, as well as the patients' clinical findings and drug history, candidates for surgery, or those who are better suited to a trial of ketogenic diet,¹⁰ are selected.

Ketogenic diet

Use of the ketogenic diet for epilepsy control dates back to biblical times.¹⁰ Over the last 20 years it has become popular again. The diet undoubtedly works although its mechanism has not been established. The literature suggests success in a third of patients. The diet requires significant support from an experienced dietician since remaining in ketosis at 3 to 4+ is essential. A 3-month trial period is recommended, after which, if the diet is tolerated and successful, it is used for 2 years, followed by a 6-month weaning period. We have had no major complications in our group of patients and growth has continued despite the strictness of the regimen.

Surgery

Epilepsy surgery may represent the only true potential cure for a child with epilepsy.¹¹ Interventions may be divided into resection (removal of abnormal tissue) and isolation (disconnection of the focus from the rest of the brain). The vagal nerve stimulator device is used in those patients with resistant epilepsy who do not have a surgical focus.¹² It is not a cure but appears to reduce seizures by up to 50% with a maximum benefit after 1 - 2 years. The device is fitted in a similar way to a pacemaker and has minimal side-effects. Parents claim that these children have better quality of life and improved mood. The main issue is the high cost, and in South Africa it is difficult to justify such expenditure within the government sector.

Genetics of epilepsy

This is a rapidly expanding field.¹³ In general most inherited (idiopathic) forms of epilepsy are relatively benign. Marked seizure type heterogeneity can occur within the same family and this highlights the need for

a detailed family tree. Such information is often withheld due to the stigma attached to epilepsy and failure to recognise odd 'blackouts' as seizures in distant family members.

Support groups

Epilepsy South Africa is a national organisation that provides immense support to children and adults with epilepsy and their carers. They offer family and individual counselling, as well as educational support to schools and community centres. They support the hospital service visiting during clinic times and attempt to link the hospital and community. Webpage:

www.epilepsy.org.za

References available on request.

IN A NUTSHELL

Childhood epilepsy is the commonest condition in paediatric neurology clinics.

Over 60% of the symptomatic causes are avoidable.

60% of epileptics have an associated neurodisability.

Over 50% of children with epilepsy do not receive medication.

The 'treatment gap' is related to lack of medical resources and stigma associated with epilepsy.

Label a child epileptic only after two seizures and then request an EEG.

A normal EEG does not exclude epilepsy.

Infantile spasms are neurological emergencies.

Epilepsy surgery is successfully practised on selected patients in the government sector.

Patients with complex or intractable epilepsy should be referred to specialist clinics.

SINGLE SUTURE

MILITARY MUSCLE

A study of over 400 000 veterans show that they have a 60% greater chance than normal of developing amyotrophic lateral sclerosis (AML). The study, by a team from Harvard, looked at men who served in the US forces in World War I and II, the Korean war and the Vietnam war. Those whose service took in more than one conflict had nearly double the risk of developing AML. The risk was independent of the military force served in. However, even among veterans, the disease is very rare, researchers stress. The cause of the increased risk is not known. About 10% of cases are inherited, but the cause of the more common sporadic form has not been identified.

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