



Introduction

Epilepsy is the tendency to have recurrent unprovoked seizures. Unprovoked means that the seizures occur 'out of the blue' for no obvious reason such as following a head injury or meningitis or low blood sugar. An epileptic seizure is caused by a sudden and abnormal burst of electrical activity from nerve cells (neurons) in the brain. Billions of nerve cells make up what is called the 'cerebral cortex'. The cerebral cortex makes up the two sides of the brain, which are called the 'cerebral hemispheres'. Each cerebral hemisphere is made up of four areas of the brain - called the 'lobes'. These four lobes are the frontal, temporal, parietal and occipital lobes.

An epileptic seizure may come from any part (lobe) of the cerebral hemispheres. If the epileptic seizure comes from one part of the brain it is called a 'focal' or 'partial seizure'. If the seizure comes from both sides of the brain at the same time, it is called a 'generalised' seizure.

Epilepsy is very common in tuberous sclerosis complex (TSC). About 65-75% of children with TSC will develop epilepsy. The reason why epilepsy occurs in TSC is because of the tubers and areas of abnormal brain development in the brains of children and adults with TSC. The tubers and abnormal areas of brain development (which are known medically as 'cortical dysplasia') contain abnormal nerve cells - which have abnormal bursts of activity and which cause the seizures.

The earliest type of epilepsy occurs in the first year of life and the type of seizure is called infantile spasms, also known as West syndrome. In fact the diagnosis of TSC may only be made after the infant has come to medical attention with infantile spasms.

The other most common seizure type in children are focal, also called partial seizures and tonic-clonic seizures.

Most children with TSC will have different types of epileptic seizure.

Although most epilepsy in TSC starts in children, it can also begin in adults. The most common seizure types in adults are focal (partial) seizures and tonic-clonic seizures.

Many children who have TSC and epilepsy also have learning difficulties and behavioural (psychiatric) problems, including autism. The earlier the epilepsy starts and the harder the seizures are to control with medication, the more likely the child will have learning difficulties and often more severe learning difficulties.

Diagnosis

The diagnosis of epilepsy depends on an eyewitness, someone who has actually seen the child have the episodes - their seizures. The eyewitness is usually the child's family who will tell the doctor about what happens in the child's seizures. This is what doctors call the 'history'. The history or description of the child's episodes or seizures is very important when making a diagnosis of epilepsy. If the history is unclear then the doctor will ask the family to try and video the child's episodes. This can be with a video-camera, camcorder or even a mobile phone. When the doctor looks at the video-recordings they will usually be able to make an instant diagnosis of epilepsy.

Once the doctor has diagnosed epilepsy the child will have a test called the electroencephalogram (EEG or brain wave test). The EEG may be undertaken with the child awake or, occasionally, when asleep. The EEG is an important test because it will help to tell the doctor what type of epilepsy the child has - the type of epilepsy is called the 'epilepsy syndrome'.

Nearly all people with TSC have abnormalities on CT (computerised tomography) or MRI (magnetic resonance imaging) brain scans. Usually these are nodules (little lumps) under the lining of the brain called subependymal nodules. Less commonly a slow growing brain tumour (called a subependymal giant cell astrocytoma - 'SEGA') may be seen on the scan. They are not usually operated on unless they cause pressure on the brain causing hydrocephalus (increased fluid in the brain). A SEGA does not usually cause seizures.

Seizure types

The following gives a short description of the most common types of seizures that occur in children with TSC.

Infantile spasms (also called 'salaam attacks'):

This is often the first type of seizure to occur in TSC. It usually starts between 4 and 9 months of age, but sometimes as early as a few weeks of age and as late as 12 months of age. Spasms that start after the age of 18 months are called 'epileptic spasms'. A spasm involves a sudden jerk - usually forwards but less commonly backwards - with the arms thrown outwards and the knees either coming up towards the chest or extending out in front of the infant. The spasm may involve both sides of the body at the same time or one side may be particularly involved. Each spasm lasts 1 to 3 seconds and may occur singly or in clusters. A cluster may last from a minute to over 20 minutes. Between 5 and 50 spasms may occur in a cluster. At the end of a cluster the infant will often

be very upset and will then be irritable for some time. Spasms usually occur soon after the infant has woken from sleep (a day-time nap or night's sleep). If the spasms have been occurring for some weeks the infant's development may slow down and they may even be thought to not see properly. Their sleep and feeding pattern may also be disrupted.

Focal (partial) seizures:

These are common in TSC. They are sometimes divided up into 'simple' and 'complex' partial seizures. Simple means that the child remains fully conscious and complex means that the child's consciousness is impaired but not completely lost.

In a simple seizure the child (or adult) may complain of an abnormal sensation or feeling. This can be an unpleasant feeling in the stomach, an unpleasant smell or taste, sudden fear or episode of *deja vu*. This is called an 'aura'. A simple partial seizure may also cause jerking of one side of the face, arm or leg whilst the person is still able to talk and interact with their surroundings.

In a complex partial seizure almost anything can happen. What exactly does happen will depend which part of the brain (which lobe) the seizure is coming from. The seizure may start first with an aura before the child (or adult) then starts to show abnormal behaviour. This abnormal behaviour may range from a slight dreaminess to complete unresponsiveness and lack of awareness. The child may show 'automatisms' which means that the child does semi-purposeful actions such as fiddling with their clothes or buttons, lip-smacking, swallowing repeatedly or mumbling incoherently. Their eyes or head may also repeatedly turn to one side. A complex partial seizure may last for seconds to many minutes. Two things may then happen at the end of a complex partial seizure. Either, the seizure will stop and then the person will be confused and may sleep. Or, the seizure may spread and progress into what is called a 'secondary generalised tonic-clonic' seizure'.

Tonic-clonic seizure:

This is the most common and also the most well-recognised type of epileptic seizure. It is also called a 'grand mal' attack. The seizure involves two phases - the tonic and the clonic phase. The seizure often starts with a sudden cry or grunt. Within a second or two, the person stiffens and if standing will fall. The jaw is often clenched and the tongue may be bitten. The eyes are turned upwards. If the bladder is full, there may be urinary incontinence (the person 'wets themselves'). This stiffening or tonic phase usually lasts 20 to 30 seconds after which the clonic (or jerking) part occurs. In the clonic part, the jerks increase in frequency, reach a peak and then start to slow down before then stopping. Over 90% of tonic-clonic seizures last 2 to 3 minutes but rarely they may last longer than 5 minutes. If the seizure last longer than 5 minutes this is often called 'convulsive status epilepticus'.

'Drop attacks' or 'drop seizures':

Different types of seizures may cause the child to suddenly 'drop' and either stumble or actually fall down. There are three

types of seizures that cause 'drop attacks'. These are 'tonic' or stiffening seizures (as if a tree has been felled), 'atonic' (as if a puppet's strings have been suddenly cut) and 'myoclonic' (as if someone has been suddenly shocked or startled). Sometimes two of these seizures may occur together, and this is often called a 'myoclonic-atonic' seizure.

Myoclonic seizure:

These are quite common in children with TSC. The seizure looks like a sudden shock or startle and can involve the whole body, one side of the body, the face or just one arm or leg. Myoclonic seizures may be focal (coming from one part or lobe of the brain - usually the frontal lobe) or generalised.

Absence seizures:

The child's consciousness is lost during this type of seizure but there are no abnormal movements. They used to be called 'petit mal' attacks but this term is no longer used. Absence seizures are very rare in children with TSC. Some children with TSC can have seizures in which they appear to be unresponsive and 'blank' and fidget with their clothes for a minute or so - but these will be focal and not absence seizures.

Epilepsy syndrome

Different types of epilepsy - called the 'epilepsy syndrome' - can occur in children with TSC. The two most common epilepsy syndromes are:

1. *West syndrome:* this is diagnosed on the basis of infantile spasms, the age at onset of spasms (under 12 months of age) and a typical EEG appearance - called *hypsarrhythmia*.
2. *Lennox-Gastaut syndrome:* this is diagnosed on the basis of different seizure types that occur in a child (particularly tonic, tonic-clonic and partial seizures), the age at onset of the different types of seizures (between 1 and 6 years of age) and a typical EEG appearance (called *slow spike and slow wave activity*).

It is important to understand that a child with TSC may start with West syndrome in the first year of life and then evolve (change) into Lennox-Gastaut syndrome in the second or third year of life.

Status epilepticus

Convulsive, also called tonic-clonic status epilepticus can be defined by the following:

- a tonic-clonic seizure that lasts longer than 30 minutes or,
- repeated tonic-clonic seizures, each lasting less than 5 minutes with the child not recovering fully between each seizure and these seizures continue for at least minutes.

Status epilepticus is a medical emergency and needs emergency treatment. If it is not treated urgently and successfully, then the child may suffer brain damage and, rarely, may die.

There are different types of status epilepticus and the other most common type which also occurs commonly in children with TSC is 'non-convulsive status epilepticus'.

In 'non-convulsive status epilepticus' the children become quieter than usual, may stop talking, drool excessively and appear to not to be aware of their surroundings. They may also have subtle head nods (atonic) or myoclonic seizures. Non-convulsive status epilepticus is common in children who have Lennox-Gastaut syndrome. Parents are usually the first to recognise that their child 'has changed' or is 'different'. The EEG is very important in making a diagnosis of non-convulsive status epilepticus. Although it is not as severe a medical emergency as convulsive status epilepticus, it does require urgent treatment.

Treatment

In general the same medicines which are used to treat any type of epilepsy are used to control the seizures occurring in TSC. Particularly helpful drugs include carbamazepine, vigabatrin (for infantile spasms), sodium valproate, lamotrigine, levetiracetam, rufinamide and topiramate. Other drugs that may be used include corticosteroids and nitrazepam for the treatment of infantile spasms (West syndrome). Treatment tends to be less effective in those with severe learning difficulties, than in those who do not have learning difficulties. One drug in the lowest effective dose should be used if possible. The recognition of un-wanted side-effects from medication is more difficult in children and particularly if the child has learning difficulties. This is because they may not be able to describe any side-effects. It is therefore important that those who care for the child should look out for any changes in their child's behaviour.

A treatment called the ketogenic diet may sometimes be helpful for children with seizures that are difficult to control by medicine. The ketogenic diet is available in three types: the 'classical', the 'medium chain triglyceride (MCT)' and 'modi-

fied Atkin's'. It is important to understand that the ketogenic diet is not a normal diet and children need to take vitamin and mineral supplements. The diet is also difficult for the family to prepare and the child to take.

Epilepsy surgery or the implantation of a vagal nerve stimulator (VNS) may be an effective treatment option for a very small number of children and adults with seizures that do not respond to antiepileptic medication.

More information on the anti-epileptic drugs (AEDs) used in people with TSC can be found in another fact sheet ('Anti-epileptic drugs: how they treat seizures and their unwanted side-effects')

Prognosis (outcome)

The outcome for children with TSC and epilepsy varies enormously. Most seizures will continue into later life, including into adult life. Although tonic-clonic seizures may become less frequent with time, focal (partial) seizures usually continue. However, there are always exceptions to this general rule. Treatment (sometimes including surgery for a very small group of children) will help to reduce the number or change the pattern of seizures, but it is unlikely that the epilepsy will ever completely 'go away'.

Epilepsy is generally more difficult to control if the child has moderate or severe learning difficulties.

Advice, information and support

Advice on all aspects of epilepsy may be found from:

- Epilepsy Action (previously called the British Epilepsy Association) - telephone 0113 210 8800
Epilepsy Helpline: freephone 0808 800 5050
e-mail address epilepsy@epilepsy.org.uk
website, www.epilepsy.org.uk

Advice and information on the different antiepileptic drugs used to treat epilepsy can be found from:

- www.medicinesforchildren.org.uk

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Further information on TSC and the work of the Tuberous Sclerosis Association can be obtained from our website at: www.tuberous-sclerosis.org

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