

So what do you do when the epilepsy drugs don't work, when your seizures continue or the side effects from the medication are beyond a tolerable level? Neurologist Dr Fergus Rugg-Gunn looks at your options and discusses when it is time to ask for a referral to an epilepsy specialist centre

## When AEDs don't work



Seizures and side effects from anti-epileptic drugs (AEDs). Either of these, in isolation or in combination, can impact on your life. But it is important not to give up hope.

As a medical profession we are very good at bandying around statistics. Up to 70 per cent of people with epilepsy gain seizure control through medication while 30 per cent have ongoing seizures. Forty-seven per cent of people achieve seizure freedom on the first drug they are prescribed, 32 per cent on the second drug, nine per cent after the third and so on.

If you are in the '30 percent' category and have already tried a cocktail of medications, the statistics offer little comfort. But statistics only tell part of the story.

Recent studies have shown that taking a nihilistic view that nothing can be done to improve seizure control in chronic epilepsy through medication is overly pessimistic. In fact with the right approach to treatment 28 per cent of those with chronic epilepsy can achieve seizure freedom while a further 50 per cent will see a significant improvement.

Even if you have been taking a variety of drugs over a period of 30 years, the newer drugs which have been licensed in the last 15 years offer real hope. Some people reach a stage where they feel a drug or combination of drugs is giving them the optimum seizure control with minimal side effects, even if it's not perfect. They may opt to stop there and that is fair enough. But if you are happy to give the newer drugs a try, all options should be explored. So where should you begin?

The first thing is to take control of your epilepsy. Today there is a two-way street with patient and doctor looking at all treatment options together.

You know how your seizures and

Ongoing seizures/  
side effects?



Find your nearest  
specialist or  
tertiary centre  
See page 20



Ask your GP  
or specialist  
for referral  
to a tertiary  
centre



medication affect you and what your priorities are. If your medication is making you feel anxious or short tempered, drowsy or depressed, make sure you tell your GP, neurologist or epilepsy specialist nurse. A minor adjustment to your dose could reduce the symptoms without impacting on your seizures. Either way these are important issues which can affect quality of life as much, if not more, than seizure control.

It is also important to discuss any other illnesses you may have and any medication or treatment you are taking. You may be seeing three or four doctors at different hospitals and good communication between them is vital. One shared electronic database across the whole NHS is a long way off, but we must still make sure there is joined up thinking.

Never assume that we know about other conditions you may have. Bring along all medication and doctors' letters to your appointment. This can help with identifying any interactions between drugs for different conditions.

If you have ongoing seizures or unacceptable side effects, you are entitled to ask for a review of your diagnosis by an epilepsy specialist at a tertiary centre. Tertiary centres are specialist hospitals or units that offer specific treatment for different conditions and referral needs to be from your GP or neurologist.

The NICE guidance (The National Institute for Health and Care Excellence) is very clear about when you should be referred to see a specialist. Uncontrolled seizures and severe side effects are both listed reasons for a referral.

I work at Epilepsy Society's tertiary service at the Chalfont Centre in Buckinghamshire. Our first priority is to consider whether or not a person's

diagnosis is correct. As many as one in three of the people we see is found to have a wrong diagnosis.

In some cases tests show that a person may not have epilepsy at all but may be experiencing non-epileptic seizures. While epileptic seizures are a result of a disturbance in the electrical activity in the brain, non-epileptic seizures have a psychological cause.

### 'Even if you have been taking a variety of drugs over 30 years, the newer drugs offer real hope'

Non-epileptic seizures are in every way as real as epileptic seizures but they do not respond to anti-epileptic drugs and the person should instead be referred for psychological support.

In other cases, although the diagnosis of epilepsy may be right, the type of epilepsy may be wrong. For example a person may have been prescribed medication for focal epilepsy whereas tests show they have generalised epilepsy. NICE has drawn up some useful guidelines and we know that certain drugs work better for different seizure types.

The toughest call is when the diagnosis is correct but the medication is not working and a long list of drugs have been tried. Here we need to look at the history of the person's medication and try to determine which have helped the most, whether any have increased the number or severity of their seizures and which have worsened or reduced side effects.

Our aim is to produce a hit list of the drugs which are most likely to be effective and those we can rule out as ineffective. Wherever possible, drug changes such as these are carried out

through our outpatients clinic, but we may admit someone to our Sir William Gowers Assessment Centre so that their medication regime can be changed in a supervised environment.

In some instances, we may use the services of our therapeutic drug monitoring (TDM) unit to look at concentration levels of specific medications in a person's blood. This is particularly useful if we are concerned that they may not be taking their medication as prescribed or if they are on three or four different drugs and we want to find out which ones may be causing severe side effects. You can read more about therapeutic drug monitoring over the page.

Too often we hear that GPs are reluctant to prescribe some of the newer drugs because they are more expensive. It is true that some of the more recent drugs which are still under patent are more expensive than the older drugs. But epilepsy drugs as a whole are not expensive in comparison with other treatments. The cost should also be looked at in the context of overall cost of patient care – visits to GPs, A&E, an overnight hospital stay. If these are reduced there are huge savings to be made. If seizures improve, costs are very quickly recouped.

One of our patients was prescribed a new medication while awaiting surgery for his epilepsy. He became seizure free and no longer had to undergo surgery. The savings there were tens of thousands of pounds.

So, don't give up. Work with your GP, neurologist, or specialist. Ask if there are any new drugs which you haven't tried and explore all options.

**Dr Fergus Rugg-Gunn is consultant neurologist at Epilepsy Society and the National Hospital for Neurology and Neurosurgery**

Is your diagnosis correct?



Are you taking the wrong drug/wrong dose?



Are your epilepsy drugs interacting with other drugs?



## Getting the best out of your epilepsy medication



Understanding how an epilepsy drug behaves in your body is a vital part of ensuring you have maximum seizure control and minimum side effects. Professor Philip Patsalos is head of Epilepsy Society's Therapeutic Drug Monitoring (TDM) unit. He answers questions about drug monitoring.

### What is therapeutic drug monitoring?

Therapeutic drug monitoring is about measuring the levels (concentrations) of epilepsy drugs in your blood so your medication can be individualised to your own therapeutic range – the level at which a specific drug works best for you, giving maximum seizure control and minimum side effects.

### How does that work?

Epilepsy drugs each have their own reference range. This refers to the range at which concentrations of the drug are most likely to work. If concentrations fall below the range, seizures are unlikely to be controlled. If concentrations are above the range, this may lead to toxic side effects. But individuals vary in their response to different drugs – some people may obtain seizure freedom at concentrations

below the reference range. This is why it can help to establish an individual therapeutic concentration which has the best results for the individual.

### That sounds quite complicated. Is it?

Not really. Our bodies are all different which means we react to and metabolise drugs differently. If five people were all given the same drug at the same dose, the concentration of that drug in their bodies would be different for each individual. The way we metabolise a drug depends on age, gender, other conditions we may have and other medications we are taking.

### So should everyone have their individual drug levels monitored?

If your epilepsy is stable your GP or neurologist may not feel TDM is necessary. TDM should not be undertaken routinely but in specific situations. These include:

- when an individual's seizures are controlled, TDM shows the ideal epilepsy drug concentration to stop their seizures. This will give a benchmark of comparison should their situation change
- if a person is still having seizures, TDM can check whether they are taking their medication as prescribed
- when epilepsy drugs are changed from one type to another, for example from a branded to a generic drug, it can be helpful to check drug concentrations in the blood before and after the change
- if someone is taking more than one

epilepsy drug or a combination of drugs for several conditions, TDM can help establish whether any dosage adjustments are needed

- in cases of suspected toxicity.

### Are there any risk groups when TDM is especially important?

Yes – children, women and the elderly. The way a child absorbs and distributes a drug will change as they get older. In women, pregnancy or the oral contraceptive pill can affect levels of drug concentration and seizure control. And under-dosing, over-dosing, missed doses and make-up doses are common in older adults which can alter drug concentrations and effectiveness.

### Are you able to check the levels of all epilepsy drugs in the blood?

We can, in fact we are the only TDM unit in the UK to be able to monitor all 25 licensed anti-epileptic drugs. We are also the only centre in the UK to be able to measure drug concentrations through saliva testing as well as blood tests. This is good news for anyone with a fear of needles, and for children, the elderly and those with learning disabilities. It is painless and less stressful.

### How can you get your drug concentration levels checked?

You can access our TDM service by referral from a healthcare professional. Find out more at [www.epilepsysociety.org.uk/tdm](http://www.epilepsysociety.org.uk/tdm) where there is also an AED level (concentration) request form for healthcare professionals.

## Therapeutic drug monitoring and pregnancy

**In 2011 the Centre for Maternal and Child Death Enquiries released a report investigating the deaths of 14 women with epilepsy during the period 2006-2008.**

**Nine of the women were on lamotrigine but blood tests were not taken to check drug concentration levels.**

**It is known that levels of the drug can fall dramatically during pregnancy and an increase in dose is often needed.**

**Dr Fergus Rugg-Gunn describes the experience of one of his patients.**

*'Jenny (not her real name) was planning to start a family. She was taking 150mg of lamotrigine twice a day and her seizures were well controlled. We decided to check her individual therapeutic range before she fell pregnant so that we had a baseline for comparison.*

*Once Jenny became pregnant, we checked the concentration of lamotrigine in her blood again, suspecting that if levels fell, she could be at risk of a seizure. As expected, her drug levels had fallen and guided by therapeutic drug monitoring, we gradually*

*increased her prescription to 250mg twice a day throughout her pregnancy. Jenny remained seizure free and gave birth to a healthy baby. After delivery her drug concentration levels were again checked and her dosage adjusted to 150mg twice a day.*

*Some epilepsy drug levels fall during pregnancy and it is important that women are monitored to ensure appropriate dosage adjustments are made to optimise seizure control. This should be carried out at least every trimester and more often if levels continue to fall.'*