# monitoring epilepsy

epilepsy society factsheet 18

If you have epilepsy, how it is managed is very important. This factsheet is about how doctors monitor epilepsy, looking in detail at therapeutic drug monitoring. Words in **bold** are explained in the summary of terms at the end.

## what is 'managing epilepsy'?

There are many parts to managing epilepsy: looking at the type of seizures you have and how they affect you, whether you take medication and if it controls your seizures, and how epilepsy affects you generally in all aspects of your life.

Managing epilepsy usually involves a specialist (a neurologist or epilepsy specialist) and your GP. You might also have an epilepsy nurse and other doctors. But you also have an important role in managing your epilepsy. This includes being involved in discussing, and making decisions about, your epilepsy and its treatment.

## what is monitoring?

Part of managing epilepsy is looking at the practical things: if you have seizures you might want to try and get them better controlled (stopped), or if your seizures are well controlled but you have side effects from the medication, you might want to know what the options are for changing this.

Managing epilepsy involves *monitoring* (keeping records of) what medication you take and how it affects you, and when you have seizures and what they are like. This is a way of seeing if your treatment is working.

## medication

The aim of epilepsy treatment is to stop seizures happening. For most people, seizures are controlled with anti-epileptic drugs (AEDs). The aim of treatment with AEDs is to stop the seizures with the smallest **dose** of the fewest number of AEDs, and with the least side effects (called **optimal therapy**).

So taking medication involves getting the right balance of the dose, seizure control and side effects. This varies from one person to another.

**See our booklet *medication for epilepsy* for more information.**

## doses and concentrations

When you take AEDs, you take a particular number of tablets, and each tablet is a certain strength (or 'size'). The strength is a measure of the amount of the **active ingredient** in the tablet. Adding the number of tablets and their strength together gives you the dose that you take every day. For example, taking two 200mg tablets twice a day is a dose of 800mg per day. The dose is a measurement of how much AED you take.

How well a drug works depends on it getting to the part of the body it needs to work on (the **site of action**). How effective it is, and how much is getting to the site of action, is found by measuring the amount in the blood (rather than just the dose that you take). This is called your 'drug concentration' or '**blood level**' and is found by doing a blood test.

The dose of AED you take will affect the concentration that is in your body, but dose and concentration are not quite the same thing. Our bodies are all different and we each react to, and **metabolise**, drugs differently. How we metabolise drugs is affected by our age, our gender, any other conditions we have and any other medications we take. So if five people all take the same dose of the same drug, they will not necessarily have the same amount of drug in their body after it is broken down.

## reference ranges and individual therapeutic concentrations

'Reference ranges' and 'individual therapeutic concentrations' are terms that doctors might use when talking about epilepsy treatment and AEDs.

The **reference range** (RR) is a **range** of drug concentrations in the body within which a drug is thought to be most likely to work. Under the lower end of the range, the AED is not likely to control seizures and above the upper end, **toxic** effects are likely. This range is not always helpful because individuals vary in how they respond to treatment.

Some people will get seizure control under the lower limit, which suggests that a lower limit is not a useful measure (only that seizure control is less likely at lower concentrations).

The **individual therapeutic concentration (ITC)** is the drug concentration which has the best result for a particular individual. Individuals will have ITCs below, within or above the reference range. Once the person's seizures are controlled, their ITC can be found by undertaking two blood tests and finding the average drug concentration from them.

## what do blood levels show?

Blood levels should be measured after you have been taking a new, or increased dose of an AED for a few days. This is called a '**steady state**' because the blood test result will be a reliable measure of their concentration.

## how are blood levels measured?

During a blood test the blood is analysed and the concentration of drug in it is calculated.

The best time to have a blood test is just before your next dose is due and you have the least amount of drug in your body. This is called the 'trough level'. Although this is the ideal time, it is not always possible: if you take your drugs at 7am and 7pm, it is hard to get an appointment just before 7am or 7pm! If the doctors know when you took your last dose they can try to work out how near your trough level you are when you have a test.

**Note**: In some cases, for example children, people with a learning disability, or people who do not like having blood taken, saliva levels can be checked instead of blood. This is a simple test and the drug levels are measured by taking a saliva (spit) sample. This test is useful for several AEDs including carbamazepine, clobazam, eslicarbazepine acetate, ethosuximide, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, primidone, vigabatrin and zonisamide.

## what is therapeutic drug concentration monitoring?

**Therapeutic drug concentration monitoring (TDM)** means using blood levels to individualise epilepsy treatment to get the best seizure control with the least side effects for each person. Measuring the amount of drug in the blood is a way of looking at the link between drug concentration and its effect on seizures (whether it stops seizures or causes side effects).

It is better to measure how effective an AED is using concentrations in the blood rather than looking at the dose taken, because not all of the AED taken (the 'dose') will get into the blood.

How useful TDM is depends on the reason it is being done (see below), how the AED is absorbed in the body and how well it works.

## when could monitoring be useful?

Although TDM is not always done, there are many situations when it can be useful in managing epilepsy.

- **When medication is started.**
  Usually, when AEDs are started, they are taken in small doses and gradually increased until they control the seizures. Often the AED dose is within a range of doses that is thought to be effective for that particular AED. This range shows the likely effective dose for 'anyone' and does not predict what dose is likely to be best for a particular individual. TDM helps to work out an expected effective concentration for an individual, depending on their individual characteristics (such as age, gender and any other medical conditions).

- **When epilepsy is controlled with AEDs.**
  When an individual's seizures are controlled, TDM shows the ideal AED concentration (their individual therapeutic concentration or ITC) to stop their seizures.

- **When someone who has been seizure-free starts having seizures again.**
  If the person's ITC is known (see above) and seizures start again, their blood levels can be checked. If their blood level is at the ITC, the seizure was not caused by a problem with the medication. If the blood levels are not at the ITC this could be the reason why the seizures have started. Blood levels can change for many reasons including starting other medications, developing another condition, or with age.

- **When someone is still having seizures.**
  AEDs work best when they are taken regularly: the right dose at regular times. There are many reasons why someone might not take their medication regularly and TDM can be used to see if this is the reason why they are still having seizures. TDM can also look at whether the person is having seizures because they are not taking enough AED, or because their body is not reacting to the AED as expected.

- **When different forms of AED are used.**
  If AEDs are changed from one form to another (for example from a **brand** to a **generic** version) this can affect drug concentrations and seizure control. TDM before and after changing AEDs can help to see if the new form is affecting the concentration in the blood.

**See our factsheet *generic and branded AEDs* for more information.**

- **When someone takes more than one AED.**
  If someone has seizures that do not respond well to taking one AED on its own, they may be prescribed more than one AED. Some AEDs interact or interfere with each other, and this can affect how well they work. If it is likely that one or more of the AEDs need to be increased because of interactions, TDM can be used to help guide the increases in dose so that the concentrations in the body are kept stable. Also, if the person has side effects or **toxicity**, TDM can show which AED is causing this.

- **To diagnose toxicity.**
  If someone starts to show signs of drug toxicity (such as being very drowsy or dizzy), blood levels can show at what concentration they react badly to the drug. TDM also helps to show toxicity in people who might find it difficult to explain how they are feeling (such as young children or people with a learning disability).

- **When someone has other medical conditions or medications.**
  Having other medical conditions, or taking other medications, can affect how AEDs are metabolised. Other medications might also interact with AEDs. Because this can affect AED levels, TDM can be used to manage any changes to AEDs that might be needed to keep the drug concentrations stable in the body.

## special situations

There are some situations where it is likely that someone will need changes to their medication. Some of these are explained below.

**Children**

How drugs are absorbed and work in a child's body changes as they get older. Generally, a child's body will metabolise (break down) AEDs quicker than an adult's. This means that children may need to take more of an AED (based on their body weight) than adults because the AED doesn't stay in their body as long. Therefore it can be hard to predict how much AED a child will need, and how this will change as they get older.

Taking other drugs alongside AEDs can cause changes in AED concentrations. TDM can help manage any changes in AEDs that are needed because of taking other medications.

Also, side effects can be different, and harder to see, in children than in adults. TDM can help to work out what amount of AED is needed for an individual and check to see if side effects are happening.

**See our booklet *medication for epilepsy* for more information.**

**Pregnancy**

Pregnancy can affect how drugs are metabolised. TDM can help to work out what effect pregnancy may have on a woman's AEDs and what changes to her AEDs might be needed to control her seizures. Also, when a woman who is pregnant takes AEDs, her baby is exposed to some of the drug. Generally, most women with epilepsy have healthy babies but TDM can be useful to keep AED levels to a minimum to reduce any exposure to the baby.

**Older adults**

Age can affect how well drugs are metabolised, and this varies from one person to another. As people get older they may develop other conditions, take other medications, or become more sensitive to the effects of medication. Older people may develop memory problems and so may forget to take AEDs, not take enough or take too much. All these things can affect drug concentrations and seizure control. TDM can help to work out the best dose to reduce side effects. Also, if seizures happen, TDM can help to work out whether this is because they are not taking the medication regularly or because their body is not absorbing it.

## should everyone be monitored?

This depends on their situation. Currently, few people have TDM as part of their epilepsy management. This might be because their epilepsy is stable, because the hospital or clinic they go to does not have the facilities, or because their doctors are not aware of how TDM can be used. Some people only have TDM if they are on phenytoin (because it is well known that this AED is unusual in how it distributes around the body, and TDM can help to check this).

If you have any questions about whether you should have TDM, talk to your GP or neurologist.

## further information

**Epilepsy Society information**
Generic and branded AEDs
Medication for epilepsy

## summary of terms

**Active ingredient** – the chemical part of a drug that makes it work.

**Blood levels (also called plasma or serum concentrations or levels)** – a measure of how much AED there is in the blood, plasma or serum. Plasma is the fluid part of blood that carries blood cells and clotting-agents (that help blood to clot). Serum is the part of plasma without the clotting agents.

**Brand name** – the name of a drug which is given by the company that makes it. The brand does not say what the active ingredient is, and there can be many brand versions of the same generic drug.

**Dose** – the amount of the drug that is taken, for example as a tablet, each day.

**Generic name** – the name of a drug that tells you what the active ingredient is. All drugs with the same active ingredient have the same generic name. One generic drug can be made by many different companies and can have many brand names.

**Individual therapeutic concentration (ITC)** – the concentration of an AED which gives the best response in an individual (optimal therapy).

**Metabolise** – breaking down substances, such as drugs, in the body so that they can be more easily removed (excreted) from the body.

**Optimal therapy** – when someone is on the best treatment for them. This means when their seizures are controlled (stopped) with the smallest dose of the fewest number of AEDs, and with the fewest possible side effects.

**Range** – a scale of something, such as drug concentrations, which has a lower and upper limit.

**Reference Range (RR)** – a range of drug concentrations that are likely to be effective for most people.

**Site of action** – the part of the body where the drug works. In the case of AEDs this is the brain.

**Steady state** – where the drug has been taken for a few days and the blood levels are a reliable measure of the concentration in the body. Steady state usually happens after about five 'half-lives' of the drug (the time taken for the amount of drug in the body to reduce by half). Half-lives vary between AEDs but if the half-life is 12 hours, steady state would happen after 2½ days (5 x 12 hours).

**Therapeutic drug concentration monitoring (TDM)** – the system for monitoring AEDs to study the relationship between drug dose, concentration and effect.

**Toxicity or toxic** – when the concentration of a drug causes harmful side effects to the person taking it.



Epilepsy Society, Chesham Lane
Chalfont St Peter, Bucks SL9 0RJ
Registered charity number 206186



epilepsysociety.org.uk

helpline
01494 601 400
Monday and Tuesday 9am to 4pm
Wednesday 9am to 7.30pm
Confidential (national call rate)