

Many women with epilepsy find that their seizures are affected by hormonal changes. Understanding the facts about this can help to improve seizure control.

Women and epilepsy

A number of different hormones in a woman's body control bone and muscle growth, heart rate, hunger, emotions and the menstrual cycle. The hormones associated with the menstrual cycle, oestrogen and progesterone, have a clearly established link with seizures. When seizures are exacerbated or occur exclusively during ovulation or just prior to or during menstruation it is termed catamenial epilepsy.



Seizures and hormones

Although hormones generally do not cause seizures, they can influence their occurrence. Oestrogen and progesterone act on certain brain cells. Oestrogen excites the brain cells and can make seizures more likely to occur, whereas progesterone may inhibit the brain cells preventing seizures in some women. This is why some women have seizures or experience changes in seizure patterns frequently at times of hormonal fluctuations such as puberty, ovulation, menstruation or menopause.

Keeping a diary is a good way to identify if hormones trigger seizures.

Puberty

Puberty is a time of complex physical and emotional changes. Fluctuating hormone levels during puberty can affect seizure control. The physical changes and growth can also happen so quickly that the dose of antiepileptic medication which worked previously may no longer be enough to control seizures. This is a good time to have antiepileptic medication blood levels checked to determine if the dose needs to be changed.

Menstruation

Women with epilepsy may have a tendency to have more seizures at certain times of the menstrual cycle.

This can be due to:

- Hormonal fluctuations
- Fluid retention
- Reduced blood levels of antiepileptic medications before menstruation
- Sleep disruption
- Stress and anxiety

Menstrual changes have been identified in 30-50% of women with temporal lobe epilepsy as compared to 7% of women without epilepsy. These can include irregular menstrual cycles ranging from several months without menstruation to prolonged or shortened menstrual cycles.

Discuss concerns about menstruation and seizures with the doctor.

Fertility

Fertility can be reduced in women with epilepsy. This means that women with epilepsy may find it more difficult to become pregnant. There are many different causes of reduced fertility. These can include having epilepsy itself, or taking certain or multiple antiepileptic drugs (AEDs) or other associated conditions such as polycystic ovarian disease.

Polycystic ovary syndrome (PCOS)

There are two conditions: Polycystic Ovaries (PCO), and Polycystic Ovary Syndrome (PCOS)

An ovarian cyst is a fluid filled sac that occurs in or on an ovary.

1. Polycystic ovaries (PCO) means multiple ovarian cysts are seen on ultrasound.
2. PCOS is a metabolic condition that may or may not come with having polycystic ovaries.

To be diagnosed with PCOS a woman needs to have 2 of the following: 1) Polycystic ovaries appear on ultrasound. 2) Irregular periods. 3) Increased male hormone in the blood test or associated symptoms such as extra hair growth or acne. So if a woman has irregular periods and an increased male hormone she could have PCOS without her ovaries being polycystic.

Although there may be some similarities in the names, the risks and medical treatments are very different for these two conditions. PCO is a normal variant of a woman's ovary, whereas PCOS is a diagnosed condition with short and long-term consequences.¹

Women with epilepsy have features of PCOS at a higher than expected rate, and PCO also are present at high rates in this population.² No clear reason has been established for this. It is important for women with epilepsy to be aware of the symptoms for PCOS. These include³:

- Excessive hair growth on the face, chest, abdomen, etc
- Hair loss, in a classic "male baldness" pattern
- Acne
- Polycystic ovaries [seen on ultrasound]
- Obesity, particularly central obesity (being apple-shaped)
- Infertility or reduced fertility
- Irregular or absent menstrual periods

Contraception

Certain AEDs can interact with hormonal contraceptives and decrease their effectiveness, leading to unplanned pregnancy. In addition, hormonal contraception can have a two way interaction with some AEDs, which can result in loss of seizure control or medication toxicity⁴. Therefore, some methods of contraception may be less effective in preventing pregnancy for women taking certain AEDs⁵. These are listed below:

Antiepileptic drugs that can interfere with contraceptives*

- Carbamazepine [Tegretol, Tegretol CR, Teril, Caramazepine Sandoz]
- Clobazam [Frisium]
- Lamotrigine [Lamictal, Elmendos, Lamidus, Lamogine, Lamotruster, Seaze, Apo-Lamotrigine, GenRx Lamotrigine, Lamotrigine generic health, Lamotrigine Sandoz, Lamotrigine-GA]
- Oxcarbazepine [Trileptal]
- Perampanel [Fycompa]
- Phenobarbitone
- Phenytoin [Dilantin]
- Primidone [Mysoline]
- Rufinamide [Banzel]
- Topiramate [Topamax, Tamate, Epiramax, APO-Topiramate, RBX Topiramate, Topiramate Sandoz, Topiramate-GA]

1 <http://www.dralexpolyakov.com.au/polycystic-ovaries-or-pcos-whats-the-difference/>

2 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1198730/>

3 <http://patient.info/wellbeing/health/polycystic-ovarian-syndrome-pcos>

4 <http://www.uspharmacist.com/content/d/feature/c/46118/>

5 <http://www.seizures.com/wp-content/uploads/2010/07/OCPs-and-AEDs.pdf>

Antiepileptic drugs that do not interfere with contraceptives*

- Acetazolamide (Diamox)
- Clonazepam (Rivotril, Paxam)
- Diazepam (Valium, Antenex, Chemmart Diazepam, Diazepam-GA, GenRx Diazepam, Ranzepam, Terry White Chemists Diazepam, Valpam)
- Ethosuximide (Zarontin)
- Gabapentin (Neurontin, Nupentin, Pendine, Gantin, Gabatine, Gabaran, Gabahexal, APO-Gabapentin, Chemmart Gabapentin, DBL Gabapentin, Douglas Gabapentin, Gabapentin Sandoz, Gabapentin-GA, GenRx Gabapentin, Terry White Chemists Gabapentin)
- Lacosamide (Vimpat)
- Levetiracetam (Kepra, Kepcet, Kevtam, Levecetam, Levitam, APO-Levetiracetam, Chemmart Levetiracetam, Levetiracetam Generichealth, Levetiracetam SZ, Terry White Chemists Levetiracetam)
- Pregabalin (Lyrica)
- Sulthiame (Ospolot)
- Tiagabine (Gabitril)
- Vigabatrin (Sabril)
- Zonisamide (Zonegran)

Antiepileptic drugs that may have a limited clinical interaction and in some people may require additional contraceptive measures*

- Sodium Valproate (Epilim, Valprease, Valpro, Valproate Winthrop, Sodium Valproate Sandoz)

* Source: NSW Medicines Information Centre - Drug Information Pharmacist 16 Feb 2011

The decision to take an oral contraceptive should be discussed with the doctor, as additional contraceptive precautions may be necessary. For women taking an AED that does not interfere with the contraceptive's metabolism, a low dose oral contraceptive, or mini pill (progestogen only) can be considered.

The morning after pill

Women who are taking antiepileptic medications may require a higher dose of the morning after pill. It is advisable to discuss this with the doctor.

Non-hormonal contraception

Epilepsy and antiepileptic medications do not hinder the effectiveness of the intrauterine contraceptive device (IUD), cervical cap, diaphragm or condom. The persona/rhythm method relies on testing urine for hormonal changes indicating ovulation. The rhythm method depends on identifying hormonal changes. As hormones can be affected by both epilepsy and antiepileptic medications, this method of contraception can be more unreliable.



It is recommended that women with epilepsy discuss contraceptive options with the doctor.

Pre-pregnancy counselling

Pre-pregnancy counselling is very important as AEDs and epilepsy management may need to be reviewed well before pregnancy to have the best seizure control on the lowest but effective dose of suitable medication. By working with your doctor you can minimise any risks to you and your baby.

This is the time to ask important questions:

Is epilepsy inherited?

Genetics are believed to play a role in most forms of epilepsy. However, surprisingly, most people with epilepsy do not have any affected relatives. The role of genetics in epilepsy is complex – many genes with a small or modest effect on risk are likely involved – so it is difficult to predict which people are at high risk⁶. Often the risk of passing on epilepsy to your child is low. Accurate diagnosis of your epilepsy may give more idea about risk. A number of types of epilepsy are passed on through families, but many forms of inherited epilepsies are often outgrown at adolescence and easily treated.

In some families, however, many people develop epilepsy, consistent with an effect of a mutation in a single gene with a strong effect on risk in the family. This is quite rare.

Genetic testing is available for several known epilepsy genes. Genetic counselling is recommended if you have concerns about this.

Can specific medications for epilepsy affect an unborn baby?

Some medications for epilepsy are associated with a higher risk of birth defects than others. Pre-pregnancy planning is essential as treatment changes may need to be made such as:

- Change of medication dose
- Change of medication type
- Withdrawal of some medication
- Adding vitamin supplements that contain folic acid

Can anything be done to minimise the risk of birth defects?

We know that not all birth defects can be prevented. But women can increase their chances of having a healthy baby by managing their health condition and adopting healthy behaviours before becoming pregnant. Make a commitment to yourself to get healthy before and during pregnancy by actively trying to plan ahead, avoid harmful substances, choose a healthy lifestyle, and talk with your doctor.

Whilst AEDs can increase the risk of birth defects, most (over 94%) babies exposed to AEDs in utero are born free from either structural or behavioural abnormalities⁷. Prior to falling pregnant it is important to have your medications reviewed so you are on the best possible medication and dose that is safest for you and your baby.

It is important to talk to the doctor and obstetrician about the likelihood of possible abnormalities and the screening tests that may be performed for detection of abnormalities.

A healthy diet, regular moderate exercise and abstaining from tobacco and alcohol will also help to minimise risks in pregnancy.

Pregnancy

If a pregnancy is planned, it is advisable to be well informed. If it is unplanned it is important not to change your medication dose and to talk to the doctor about the pregnancy as soon as possible. In brief:

- Over 93% of women with epilepsy can expect to have normal pregnancies and healthy babies.
- Approximately 25-30% of women with epilepsy will have an increase in the number of seizures during pregnancy. However, most women will see no change in their seizure frequency.
- Women who have a link between menstruation and seizures tend to have less seizures during pregnancy

6 <http://www.ilae.org/Commission/genetics/documents/GeneticsPamphlet-2013.pdf>
7 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2970517/>

- It is desirable to establish the best possible seizure control before falling pregnant.
- There is little evidence that focal or absence seizures result in increased risk to the unborn baby.
- Tonic clonic seizures, however, can be potentially harmful to both mother and baby.
- It is preferable, but not always possible, to take only one AED. Both a neurologist and obstetrician will be involved in reviewing the medications.
- The treatment objective is to maintain control of seizures throughout pregnancy by using AEDs in such a way that the risk of unwanted side effects to mother and the foetus are minimised.
- As folic acid is thought to reduce the risk of birth defects, it is advisable to take a recommended dose (5mg/day) before conception and for the first three months of the pregnancy.
- Since the absorption of AEDs may change during pregnancy, it may be necessary to monitor blood levels and adjust medication.



Women are invited to enrol with the Australian Pregnancy Register for Women to assist with research into antiepileptic medication and pregnancy. For more information call 1800 069 722 (free call).

Breastfeeding

Most mothers wish to breastfeed and are usually encouraged to do so.

The presence of AEDs in breast milk rarely causes problems to the baby. Studies have shown that the concentration of AEDs delivered to the foetus during pregnancy is higher than that delivered to babies through breast-feeding⁸. However, if your baby continually appears drowsy, seek specialist advice.

Breastfeeding can be a tiring process and lack of sleep may trigger seizures in some mothers. These aspects should be fully discussed with your doctor.

Being a parent - tips

- Caring for a new baby is tiring, especially if the baby wakes often at night. As lack of sleep may trigger seizures, a daytime nap may be helpful.
- If you are having seizures, it may be safer to feed and change the baby on the floor.
- If alone, sponge wash rather than bathe baby.
- Always use a safety harness when baby is in a pram or stroller.
- Should you have a seizure, the usual fire-guards, play pens and stair gates will protect the child from dangers in the home.
- Consider attaching toddler reins to your wrist until your child understands the importance of staying near you (should a seizure occur).
- Children love to mimic adults, so store medications in child-proof containers safely out of reach at all times.
- As your child gets older, it is important to discuss your epilepsy with them. Storybooks are available that may help you explain your epilepsy to your children.

Menopause

A woman goes through menopause when the ovaries stop releasing eggs, causing the body to stop making natural hormones. This can bring about symptoms such as hot flushes and mood swings which are sometimes managed with hormone replacement therapy (HRT). HRT contains either oestrogen or a combination of oestrogen and progestogen.

8 <http://www.medscape.org/viewarticle/829289>

Epilepsy is known to be hormone sensitive, and oestrogen is known to affect seizures for some women. The amount of oestrogen HRT contains is small and often not enough to trigger seizures, however, many women with epilepsy do reported an increase in seizures once commencing HRT.

If you take HRT and find you are having more seizures than usual, it may be related and you will need to discuss this with your neurologist to consider possible alternatives or different combination of HRT oestrogen and progesterone. Also bear in mind that some anticonvulsant levels may be lowered by the HRT⁹.

The effect of menopause on seizures has not been the subject of extensive research. At this stage the effects cannot be well predicted. But because there are changes in the hormones produced by the ovaries, oestrogen and progesterone, it is likely this will affect seizures in some way. For some women seizures may stop while others may experience an increase in seizures, many women have no change in seizure frequency. One study showed that women who have catamenial epilepsy tend to have more seizures in the peri-menopausal period and then less seizures post-menopause¹⁰.

Menopause can create sleep problems and quality of sleep, especially in women with hot flushes. Sleep problems increase significantly as women move from pre-menopause to peri-menopause. This can also affect seizures.

Epilepsy can begin at any age and may even begin during menopause. Preliminary research has raised the possibility that some women may have a greater risk of developing epilepsy during menopause. This is more likely to be related to stroke.

Menopausal women with epilepsy have an increased risk of osteoporosis.

The role of HRT in preventing osteoporosis is particularly important for women with epilepsy. Some AEDs can reduce bone density and some people with epilepsy are at risk of falls, and therefore at higher risk of bone fractures. Bone density testing may be recommended if you are on certain types of AEDs.

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9 https://my.clevelandclinic.org/health/transcripts/viguera_menopausal_women_with_epilepsy
10 <http://www.ncbi.nlm.nih.gov/pubmed/10528936>