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Being a woman, having epilepsy

Key points

- ◆ Epilepsy can affect the timing and regularity of menstruation.
- ◆ The menstrual cycle can also have an effect on epilepsy; about 12% of women have seizures tightly linked to their menstrual cycle.
- ◆ The fertility of women with epilepsy is probably less than women in general.
- ◆ Up to 20% of women have more ovarian cysts (follicles) than thought usual, and this can be due to a condition called the polycystic ovary syndrome.

An important general point

Let's start with an important warning; this section will only apply to some women, some of the time. Many women with epilepsy sail through their periods, their pregnancies, and their eventual menopause with no problems at all even if they are taking the medication that theoretically may not be the best for them. They are the lucky ones. Almost all women with epilepsy in the developed world take anticonvulsant medication so it is sometimes difficult to decide if it is the epilepsy itself or the medication being taken for the epilepsy that poses the potential problem.

Epilepsy and the menstrual cycle

Epilepsy itself can affect the timing and regularity of the menstrual cycle and possibly fertility; to what extent is open to question. We know that after tonic clonic and complex partial seizures there is a measurable (and potentially diagnostic) release of the hormone prolactin; since this involves production in the pituitary gland and the hypothalamus other hormones and their precursors may be released as well which potentially can upset the delicate and interlocking mechanisms of the menstrual cycle. A recent and comprehensive study in

the UK certainly suggested that the fertility of women with epilepsy is less than that of women who do not have epilepsy.

What is the polycystic ovary syndrome (PCOS)?

A woman with a normal menstrual cycle sheds the lining of her womb (menstruates) roughly every 28 days. A new lining (the endometrium) then develops and grows ready to receive a fertilized egg (ovum): the ovum itself is released from one of the ovaries at about day 14 of the cycle. Several follicles (cysts) have begun to develop in the ovary towards becoming an ovum but most never get that far, die, and are reabsorbed back into the ovary. If the released ovum is not fertilized by a male sperm it dies and the endometrium is shed again; if it is fertilized then the endometrium develops further and eventually becomes the placenta that nourishes the fetus in the womb. In a normal ovary there are no more than 10 cysts visible at any one time in the various stages of development and decline; in a polycystic ovary there are more than 10. A woman with too many cysts in her ovary is said to have 'polycystic ovaries'. If, in addition, she has hormone changes (measured if possible between days 2–6 of the cycle when levels are normally at their lowest) of a raised follicle stimulating hormone (FSH), and/or a raised luteinizing hormone level (LH), and/or a raised testosterone hormone level then she is said to have PCOS, present in 4–5% of women and often, but not invariably, associated with overweight, irregular periods, and relative infertility.

A recent Birmingham study showed that women who had primary generalized epilepsy and who were taking and had only ever taken a single anticonvulsant (either sodium valproate, lamotrigine, or carbamazepine) were more likely to have polycystic ovaries than women of the same age who did not have epilepsy (the control group). But it was only the women taking sodium valproate and who were not taking 'the pill' (which is protective against the syndrome) that were significantly more likely to have PCOS when the hormone level tests for this condition were measured. It is important to emphasise that not every woman taking sodium valproate is going to develop PCOS; other factors are involved. But it is one of the reasons why women of childbearing age should avoid this drug if possible.

PCOS was first described in the late 1930s in a group of American women who were overweight, hirsute, and relatively infertile with irregular or absent periods. Our knowledge of both the syndrome and its possible causes has increased as our ability to scan the ovary safely inside the pelvis and measure the level of various hormones has increased; but practice has not always entirely caught up with knowledge. The prevalence of polycystic ovaries in women without epilepsy has been described as being between 4–19% of potentially fertile women. It is important to remember that not all women with the syndrome are hairy, overweight, and with irregular menstruation; some women with the full syndrome are of normal weight and apparently normal menstruation but have disordered hormones.

The importance of the full syndrome is not just the effect it can have on fertility, important as that is, but also that women with it are particularly likely to develop type 2 diabetes in later life (and possibly be more prone to ovarian cancer).

Why might women taking valproate sometimes have PCOS?

It may be connected to the fact that sodium valproate is known to have an effect on the metabolism of the pancreatic hormone insulin (lack of which causes diabetes). Insulin is involved in mediating ovarian function and in the causation of PCOS. Further Birmingham experience suggested that switching women with PCOS to another effective anticonvulsant and withdrawing the valproate led to the signs and symptoms of the PCOS disappearing and ovarian function returning to normal; the anticonvulsants used were levetiracetam and lamotrigine.

Does the menstrual cycle affect epilepsy or its frequency?

Sometimes, but the answer is not completely straightforward. Some simple generalized absence epilepsies may disappear in female children at about the time that menstruation starts; but this may be no more than co-incidence as similar epilepsies stop in male children at about the same time.

However, some epilepsies probably do start at the same time as menstruation and become associated with the menstrual cycle, and may stop, or greatly diminish in frequency, during pregnancy and after the menopause. There is no doubt that in some women with epilepsy there is a close and tight relationship between the frequency of seizures and particular phases in the cycle. The problem is that the views of women with epilepsy and the views of physicians as to how commonly this association occurs vary greatly.

According to two recent studies, what can be said with some confidence is that between 10–12% of women with epilepsy have seizures in which all, or the vast majority, occur at a definite time in a regularly occurring menstrual cycle. This is almost always toward the latter end of the cycle just before or at the start of menstruation although there is a small number of a woman whose peak seizure frequency occurs at, or just before, ovulation in the middle of the cycle.

What can be done about it?

It is usual to record seizure frequency and the menstrual cycle over 2 or 3 cycles—more if they are irregular. If it is then clear that a woman's seizures are related to her menstrual cycle:

- ◆ Sometimes regular anticonvulsant medication is enough; or taking clobazam or acetazolamide for up to a week at a defined point in the menstrual cycle can help.
- ◆ Hormone treatment like 'the pill' or the progesterone injection may be helpful (providing eventual pregnancy is not an issue), although rarely 'the pill' can worsen seizure frequency (see Chapter 11).

- ◆ Temporarily increasing the amount of anticonvulsant normally taken may rarely help, as can taking oral progesterone in the latter half of the menstrual cycle.
- ◆ Clomiphene has been suggested as a treatment for premenstrual seizures; this should only be used by experts as it can sometimes cause seizures.
- ◆ Switching off the menstrual cycle, with drugs such as goserelin, has also been recommended and does work, but can only ever be a temporary solution, as it is not usually prescribed for more than 6 months at a time.

The treatment of premenstrual seizures should be discussed with a medical advisor, as different patients will need different solutions (and the same patient may need different solutions at different times in her life).

Case study

Sylvia had her first tonic clonic seizure shortly after waking on the day of a maths exam at school ('I was never very good at it' she explained). She was swiftly investigated, given valproate, told she had juvenile myoclonic epilepsy, and that she would have to take anticonvulsants for the rest of her life.

She married at 25, continued to take 'the pill' until she was 28 and then stopped it to have a family. Some months after stopping 'the pill' her periods became very irregular and she often only had two or three a year but was told that was 'just her cycle'. After 11 years, at the age of 39 she still had not conceived (although her irregular cycle had raised the hope of pregnancy several times). She eventually requested specialist referral to an infertility clinic that had a contiguous epilepsy clinic.

Her EEG contained some generalized spike wave activity, particularly on overbreathing. MRI of her brain was normal, but MRI of her pelvis was not demonstrating severe polycystic ovaries: raised hormone levels demonstrated that she had PCOS. She was advised to switch to lamotrigine, which she did far more rapidly than the clinic intended—'time isn't on my side', she explained.

After being on lamotrigine for 6 months her periods became regular and her hormone levels had returned to normal. She was taking 5 milligrams of folic acid and conceived naturally and was seen in a joint obstetric/epilepsy clinic with regular blood level and EEG monitoring. At 38 weeks she chose to have an elective Caesarean section and had a healthy boy. She became pregnant again a year later delivering another healthy boy. She continues to take folic acid, chose not to breastfeed, sharing bottle feeding with her partner and at 44 is contemplating another pregnancy; 'I might have a girl, next time' she says, with a gleam in her eye—'I have a lot of catching up to do'. She has been advised to stop taking folic acid when she has decided that she has had enough children.