

**PRIMARY CARE
GUIDELINES**

FOR THE

**MANAGEMENT OF
FEMALES WITH
EPILEPSY**

Epilepsy Guidelines Group

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Introduction

Epilepsy is a condition that can affect anyone at any time. It is not a 'disease' in itself, but is the outward manifestation of other underlying conditions. The cause is often unidentifiable, although modern imaging techniques are rapidly increasing the ability to identify the cause in more patients.

Epilepsy is the most common serious neurological condition and is no longer considered to be benign. In the UK it affects more than 300,000 people, with an overall incidence of about 5–10 cases per 1000 persons and a lifetime prevalence of between 2–5% of the population. Premature death is 2–3 times higher in people with epilepsy, and 1000 die each year as a direct result of their seizures. Sudden unexpected death in epilepsy (SUDEP) is the principle cause of death, and seizure control is key to minimizing this risk. Women of childbearing years account for 25% of all people with epilepsy and most of these women will require long-term treatment with antiepileptic drugs (AEDs). It is estimated that 3-4 pregnancies in every 1000 occur to women with epilepsy: in the UK alone, around 1800-2400 infants are born every year to women with epilepsy.

These guidelines, based on a round table discussion held in London in December 2003 and sponsored by Sanofi-Synthelabo, have been written to help the non-specialist address the specific needs of women with epilepsy presenting in the course of their normal work, and are intended to help in determining those who need referral to an appropriate specialist – they are not meant as a definitive guide for the treatment of women with epilepsy. Their publication is timely in view of the guidance from NICE on antiepileptic medication in children and adults and the impending NICE guidelines on epilepsy. For GPs signed up to the new GMS contract, these guidelines may help them address the needs of women with epilepsy, which annual audit of their patients will identify.

Even with today's medical advances, there are misconceptions surrounding epilepsy, and for some people with epilepsy these misconceptions can lead to a feeling of stigma, which can in turn affect their social functioning and psychological well-being. The diagnosis of epilepsy should therefore not be undertaken lightly. Reassuringly, once the diagnosis has been made, some 70-80% of patients will have their seizures well controlled with one of the increasing number of AEDs available.

For the doctor managing epilepsy, different patients present different management challenges. Although there are important general considerations for different patient groups, it is vital to consider the needs of the individual and how these needs may evolve over time. This could not be better illustrated than in the management of women with epilepsy, particularly surrounding the choice of medication for those who are likely to become pregnant.

Making a diagnosis and goals of therapy

All females who experience an unprovoked suspected seizure must be referred to a specialist with an interest or competence in epilepsy, as defined at primary care trust (PCT) level; this may be, for example, a paediatrician, neurologist, geriatrician or psychiatrist. The patient should be seen within 28 days (although it is recognized that the current average waiting time for a first appointment with a specialist is 4 months). Some specialists operate fast track clinics for quick access and, where available, this should be sought for all new patients awaiting diagnosis.

Diagnosis of epilepsy by an epilepsy-competent service is paramount before any consideration is given to therapy, and care should be taken not to apply the label 'epilepsy' to anyone until they have been formally assessed by a specialist. It is worth noting that up to 50% of patients referred to secondary care with suspected epilepsy do not have the condition (with syncope being most commonly mistaken for epilepsy), and up to 20% of those being treated with antiepileptic drugs (AEDs) have been misdiagnosed with epilepsy. A diagnosis of epilepsy may have profound psychological, social and financial implications for an individual, e.g. ineligibility to drive and potential unemployment, low self-esteem and discrimination.

Most investigations for epilepsy are undertaken in secondary care. The GP's primary responsibility is to take a detailed history from his/her patient of the events before, during and after the suspected seizure, and to pass this on to the specialist. The referral letter should also record past contact with relevant services, relevant investigations, comorbidity and whether the patient has been advised to stop driving. The GP should stress to the patient the importance of taking an eyewitness to the specialist appointment; failing this, the eyewitness should submit a written account of what happened (see page 17 for a list of the important questions relating to the characteristics and circumstances of the 'seizure').

The GP should, at the first presentation, raise the issue of safety and the risks associated with bathing, driving, swimming and other high-risk activities, and *it should be documented in the notes that this advice has been discussed*. This advice is based on an event, i.e. unexplained suspected seizure, rather than a diagnosis, but patients must be aware that certain activities can put them at risk if they have a subsequent seizure. Drowning, for example, is not uncommon in patients experiencing a second seizure in the bath, and showering is therefore advised. Also, the patient must not drive while waiting to see a specialist. The risk of a recurrence after a single seizure is approximately 30% over the following 6 months.

The interval between presentation to their GP and the specialist appointment is likely to be a time of uncertainty and raised anxiety for patients. They will frequently request additional information and support, and it is appropriate to give them details of national epilepsy helplines and charities (see page 19).

The goals of therapy for a patient with confirmed epilepsy are easily summarized as: complete freedom from seizures, no side-effects, no mortality or morbidity, and no impact on quality of life, all achieved using the least medication required.

KEY PRACTICE POINTS

- All females who experience a suspected seizure must be referred and should be seen within 28 days by a specialist with a special interest or competence in epilepsy, as defined at PCT level.**
- The importance of taking an eyewitness to the specialist appointment who can clearly describe the 'seizure' must be stressed to the patient.**
- Risk and safety precautions should be addressed by the GP at the initial presentation and *the advice given to the patient should be documented.***
- Patients should be directed to where information and support can be obtained while waiting to see the specialist (e.g. epilepsy support groups and helplines).**
- Goals of therapy are to achieve complete seizure freedom without side-effects or impact on quality of life, using the least medication that is necessary.**

Which groups of women are of concern?

Active epilepsy has a prevalence of 4–10 per 1000 population and half of these individuals will be female. There are unique issues in the management of women with epilepsy that largely relate to the effect of female hormones on the condition (oestrogen is known to have a proconvulsant action, and progesterone an anticonvulsant action), and to the effects of epilepsy and AEDs on female sexuality, fertility, family planning choices, pregnancy and the menopause.

Epilepsy is often a lifelong condition, and women with epilepsy present a continuum of specific challenges that change with age and circumstances, from the woman of reproductive age seeking contraception or planning a pregnancy, to the postmenopausal woman enquiring about hormone replacement therapy (HRT). The GP is in the unique position of supporting a woman with epilepsy throughout the different stages of her life and is pivotal in ensuring that she receives seamless care, including counselling; he/she needs to be proactive in anticipating a woman's changing needs and circumstances and in providing timely advice and referral to meet these needs. For example, regularly raising preconceptual issues well before a woman becomes pregnant should maximize the chances that she embarks on a pregnancy well informed, well prepared and with the minimum of risk to herself and her baby. Antenatal information and guidance on the safe care of a baby for a mother who has epilepsy may help to promote confidence and reduce anxieties once the baby is born, and should minimize risk to both the mother and baby.

Adolescence is a time when females are often lost to follow-up, whether seizure-free or still having seizures. The handover from paediatric to adult epilepsy services is often haphazard as it is unusual for there to be a formal arrangement for the transfer. The GP needs to be particularly vigilant in ensuring that adolescents, who will be at the start of their sexual lives, receive appropriate care and information. The difficult issues of contraception and preconceptual counselling may not have been introduced by paediatric colleagues, and the GP may be better placed to approach these.

The effect of the menstrual cycle on seizure control is still poorly understood. Many women feel that their seizures cluster around the time of menstruation (catamenial epilepsy), but the evidence for this is poor.

Women with epilepsy may have reduced fertility, but again the evidence is far from clear-cut. It is possible that the observed lower fertility in women with epilepsy may be explained by social and economic factors rather than the effects of seizures or AEDs.

There is little literature on the effects of the menopause on epilepsy, and conversely the effects of epilepsy on the menopause. HRT is not contraindicated in women with epilepsy.

There is some evidence to suggest that women with epilepsy may be susceptible to osteoporosis; if so, the risk of fracture will be compounded by the fact that some types of

seizure increase the risk of falls and other injuries. Again, the role of AEDs in this process has yet to be clearly established. It is recommended that women with epilepsy and a family history of osteoporosis, or those who have had a fracture premenopausally, be referred for bone densitometry.

The other major issues for women with epilepsy – contraception, preconceptual counselling and planning a pregnancy, and the management of pregnancy and the postpartum – are discussed in the following sections.

It should be remembered that the incidence of epilepsy in individuals with learning disabilities is high. These individuals are entitled to receive the same level of access to specialist care and supporting information (in a format suitable for them) as other patients; this applies equally to their relatives and carers, who may need particular consideration.

With the introduction of the new GMS contract on 1 April 2004, GPs are expected to compile a register of patients receiving drug treatment for epilepsy, and to review them annually, recording their seizure frequency and date of last seizure, and they should aim to achieve seizure freedom in at least 70% of patients (see page 20).

The priority for referral of women with epilepsy should be:

- Women with continuing seizures, unless already being seen by a specialist (absolute priority).
- Women without a clear diagnosis of epilepsy made by an epilepsy-competent service.
- Women who have been seizure-free for several years and who actively want to consider stopping medication.
- Women experiencing acute or chronic side-effects on AEDs.
- Women of childbearing age if considering pregnancy.

KEY PRACTICE POINTS

- There is a continuum of unique issues in the management of women with epilepsy that will change with age and circumstances – fertility, contraception, preconceptual counselling, management of pregnancy and risk to the developing fetus, and the menopause.**
- GPs need to be proactive in anticipating the changing needs and circumstances of their female patients with epilepsy.**
- GPs need to be vigilant that adolescent girls are not lost to follow-up during the transition from paediatric to adult services.**
- HRT is not contraindicated in women with epilepsy.**
- Women with epilepsy should be referred for bone densitometry if they have a family history of osteoporosis, or a fracture premenopausally.**

Medication

Most newly diagnosed women with epilepsy should be prescribed medication by a specialist, and subsequent modifications to AED dosage and regimen should also generally be made by a specialist. However, as patients will undoubtedly seek guidance from them, GPs need to be familiar with the issues surrounding the choice of medication and the potential acute and chronic side-effects, and should aim to minimize these by gradual introduction and careful titration of AED therapy.

Of the drugs licensed for use as monotherapies, there are five to choose from that are considered suitable for newly diagnosed patients – carbamazepine, lamotrigine, oxcarbazepine, sodium valproate and topiramate. The choice of medication is governed by the potential efficacy in an *individual* patient, which in turn is governed by the seizure type and the risk of potential adverse effects in that patient. Professionals who advise women on the relative merits of the various monotherapies available should be fully aware of the potential impact of each AED and be skilled in informing patients in a way that enables them to make a balanced and informed choice; this process, which has parallels with the choices all women make regarding contraception, may take time and may have an enormous influence on adherence. Women with epilepsy should also be encouraged to seek information from other sources such as the national epilepsy charities. A woman's reasons for choosing a particular drug should be documented and the importance of adherence should be explained and stressed.

It is important to inform a patient that the choice of medication can be revisited, and indeed may need to be if the first drug of choice fails. Thus, the debate over which drug offers the best 'fit' between efficacy and side-effects for an individual patient should never become polarized between the 'perfect' drug and the 'harmful' drug, as the latter may need to be tried if the 'perfect' drug fails to control seizures or induces intolerable side-effects.

The specialist should follow up all newly diagnosed patients at an early stage to review if they are seizure-free. If one monotherapy drug fails at the maximum tolerated dose, it is practice to try another drug as monotherapy. However, in the event of failure, it should be checked that this is not due to non-adherence, and this may also be an opportunity for the specialist to reassess the diagnosis. If the second choice monotherapy drug fails, single drug therapy is still preferable but a second, 'add-on' drug should be tried – e.g. topiramate or levetiracetam. (In practice, when add-on drugs are effective, it is not unusual in some cases for the monotherapy drug subsequently to be removed.)

Monitoring AED levels is common practice in primary care (and also by junior hospital doctors). However, drug levels should *never* be used as a guide to dosing, as this may lead to dose elevation in the patient with controlled seizures who has a low blood level (which serves only to increase the risk of side-effects), and dose reduction in the patient who tolerates high

levels (resulting in seizure breakthrough). In primary care drug levels should only be checked if there is concern about adherence or toxicity. (The exception to this rule is the need for the monitoring of phenytoin levels, especially when changes to dosage are being considered; the drug's narrow therapeutic window and saturation kinetics mean that small dose increases may have large effects on serum level.) Remember that it is *the individual patient who should be treated and not the drug level* – if the patient has toxic symptoms, the drug level will need to be reduced, and if the patient continues to have seizures but no side-effects, the dose should be increased. The annual review will provide an opportunity to identify patients who are receiving toxic or subtherapeutic doses.

Routine monitoring of liver function tests (LFTs) and urea and electrolytes (U&E) is also generally unnecessary, except in at-risk groups (those with Gilbert's syndrome, patients under 2 years old, the elderly and the potentially hyponatraemic); however, it is recommended in the manufacturers' data sheets that LFTs should be monitored in the first 6 months of treatment.

Women who present with concerns about the AED they are taking, or whose needs or circumstances change, should be referred for specialist review and advice. The GP should emphasize that medication should never be stopped abruptly, and should encourage the patient to continue to take her medication until a specialist has been consulted.

KEY PRACTICE POINTS

- Women with epilepsy should feel supported and empowered to enable them to make an informed choice regarding their antiepileptic medication: this is key to adherence.**
- Generally, GPs should not be responsible for starting or changing antiepileptic medication, but they need to be familiar with the issues surrounding choice of medication in women.**
- Drugs licensed for use as monotherapies and considered suitable for newly diagnosed patients are carbamazepine, lamotrigine, oxcarbazepine, sodium valproate and topiramate: the choice of monotherapy drug is about achieving the best fit between efficacy and tolerability in an individual patient.**
- Patients should be informed that their first choice drug may fail, and that a second monotherapy drug may need to be tried.**
- If the second monotherapy drug also fails, a second 'add-on' drug will be tried (e.g. topiramate or levetiracetam).**
- Drug levels should never be used as a guide to dosing (with the exception of phenytoin, for which levels should be measured annually): GPs should only check levels if concerned about adherence or toxicity.**
- If a woman presents with concerns about her medication, she should be referred to a specialist, and the GP should continue to advise and support her to keep taking her medication in the interim.**

Contraception

Talking through the panoply of contraceptive options with women and giving them the necessary information to allow them to make an informed choice about contraception is familiar ground for GPs. However, information and guidance on effective contraception has additional importance for women with epilepsy because an unplanned pregnancy may place the woman and her developing fetus at risk. Also, there are a few special considerations regarding contraception in women with epilepsy that depend on the type of AED they are taking.

There are no contraindications to the use of non-hormonal methods of contraception in women with epilepsy. If, however, a hormonal method of contraception is preferred, she should be informed that its efficacy may be affected by the type of AED she is taking for seizure control. Non-enzyme-inducing AEDs – gabapentin, lamotrigine, levetiracetam and sodium valproate – have no effect on contraceptive efficacy. Efficacy of hormonal contraception, however, is reduced by the hepatic enzyme-inducing AEDs – carbamazepine, ethosuximide, phenobarbitone, phenytoin and primidone. Whether oxcarbazepine should be classified as an enzyme-inducing drug is still being debated; topiramate, which until recently was classified as an enzyme-inducing drug but about which there is also continuing debate, may only reduce contraceptive efficacy at high doses.

Women using an enzyme-inducing AED who wish to use hormonal contraception should be advised to consider a higher dose combined oral contraceptive pill (COC) or the injectable progestogen-only contraceptive, Depo-Provera (Pharmacia). Lower dose progestogen-only methods – progestogen-only pills and the implant, Implanon (Organon) – have a higher failure rate with AEDs and are not recommended.

Depo-Provera can provide convenient, reliable contraception for women on enzyme-inducing AEDs. By convention, the injection interval is commonly reduced from 12 to 10 weeks; however, serum levels do not appear to be reduced and the manufacturer's data sheet recommends a 12-week interval as for all other women.

Women taking enzyme-inducing AEDs who wish to use combined oral contraception should use a pill containing 50 µg estradiol or mestranol – Norinyl-I (Pharmacia) contains 50 µg of mestranol and is the only 50 µg COC currently available in the UK. It is also common practice to make up a 50 µg dose COC by taking two low-dose pills together. In this way women can also increase to a 60 µg dose if breakthrough bleeding suggests that a 50 µg dose is insufficient for good cycle control. Even on higher dose COC, women on enzyme-inducing AEDs are at increased risk of pregnancy. It is also therefore recommended that they reduce this risk by tricycling pills and by reducing the pill-free interval to 4 days, and also by using additional barrier contraception. Even with all these extra precautions, women on enzyme-inducing AEDs using the COC are still considered to be at increased risk of pregnancy. On this

basis, the COC should not be a first-line choice for women with epilepsy, although the failure rates of 7% are still lower than those with barrier methods alone (15–20%).

The progestogen-only pill and implant are both low-dose methods and would have an unacceptably increased risk of contraceptive failure in women on enzyme-inducing AEDs. They are not recommended, but if used in this situation should certainly be combined with barrier methods.

Emergency contraception can be used as normal by women using non-enzyme-inducing AEDs. Women on enzyme-inducing AEDs conventionally take a higher dose of hormonal emergency contraception: two tablets of levonorgestrel (1.5 mg) followed by one tablet 12 hours later (0.75 mg). An IUD is very effective for post-coital contraception up to 5 days after the event and should always be mentioned as a more reliable option than hormonal emergency contraception.

KEY PRACTICE POINTS

- Women with epilepsy need information about all methods of contraception to help them to choose the most suitable method for them and their partner.**
- Planned pregnancies are of the utmost importance in women with epilepsy.**
- There are no contraindications to the use of non-hormonal methods of contraception in women with epilepsy.**
- There is no change to the failure rate for oral contraceptives in women taking non-enzyme-inducing AEDs.**
- The combined oral contraceptive pill is not first-line choice for women using enzyme-inducing AEDs (e.g. carbamazepine, ethosuximide, phenobarbitone, phenytoin and primidone). However, if a woman prefers a hormonal method of contraception, she must be advised that contraceptive efficacy may be reduced: the COC will need to be tricycled with a pill-free interval of only 4 days, taken at a higher dose and combined with barrier methods.**
- Depo-Provera is recommended for women using enzyme-inducing AEDs and it can be given at the standard 12-week interval.**
- Progestogen-only pills and the contraceptive implant have higher failure rates in women taking AEDs and cannot be recommended.**
- For emergency contraception, an IUD is the most reliable choice and should be mentioned. Women on enzyme-inducing AEDs who wish to take hormonal emergency contraception should take a double dose.**

Preconceptual counselling and planning a pregnancy

Approximately 25% of people with epilepsy are women of reproductive age, and 1 in 200 women attending antenatal clinics are receiving AEDs. For women with epilepsy the message regarding having a family should be positive and reassuring. The overwhelming majority will be able to conceive and will have uncomplicated pregnancies, delivering healthy babies and bringing them up without undue problems. However, a pregnancy in a woman with epilepsy is medically complicated and requires careful ongoing management as seizures may increase in frequency or change in type during the pregnancy or after birth, placing both the woman and her baby at risk. Both seizures during pregnancy and AED exposure in utero are thought to influence the poorer outcomes seen in children born to mothers with epilepsy. AEDs have been associated with a 2- to 3-fold increase in major congenital malformations in children exposed to AEDs in utero compared with the general population (overall 3–9% compared with a background rate of 1–2%). Major congenital malformations include cleft lip/palate, spina bifida and heart defects, while minor anomalies include dysmorphic features and digital abnormalities. There are also concerns regarding growth retardation and learning disabilities.

Women with epilepsy should be offered comprehensive preconceptual counselling to allow them to make informed decisions about minimizing the risk factors for themselves and their baby. GPs should introduce preconceptual issues soon after diagnosis (or in adolescence if the patient was diagnosed as a child), well in advance of when a woman may be planning to start a family, and these should be raised at every opportunity and documented as having been discussed.

Preconceptual counselling aims to raise awareness among women with epilepsy that the best outcome for any pregnancy may be secured if the pregnancy is planned, as this will allow the necessary time for antiepilepsy medication to be optimized and seizures to be controlled before conception, with seizure freedom being the aim. It also aims to minimize the chances that a woman presents only once she finds that she is pregnant, and possibly on an AED regimen associated with a significantly increased risk of birth defects. GPs should, however, consider the possibility of pregnancy in all patients of childbearing age, and raise this at each review.

All women with epilepsy actively planning a pregnancy, or at risk of becoming pregnant, should be referred for a specialist review of diagnosis and treatment and to a preconception clinic, if available; other sources of information may also be helpful (see page 19). Abrupt withdrawal from, or changes to, medication should never be made as these modifications take time and should generally be made only under specialist guidance.

If a woman has been seizure-free for 2–3 years, she should be offered the opportunity to

discuss with a specialist the gradual withdrawal of her AED medication. This, however, may not be the woman's choice because it will have implications for her eligibility to continue to drive and may affect her employment and other lifestyle issues. DVLA recommends that patients undertaking planned withdrawal of AED medication should be strongly advised not to drive during the period of withdrawal and for about 6 months after cessation of treatment. They also recommend that when one AED is to be substituted for another, the advisory 6-month period off driving need not apply – it is suggested that a suitable observation period off driving (e.g. a few weeks) be recommended until the new treatment is satisfactorily established. Of course, if the woman has a seizure during or following withdrawal from her medication, her ineligibility to drive will be for longer (licences can only be restored after 1 year of seizure freedom or 3 years of uniquely nocturnal seizures).

If withdrawal of AEDs is not an option, or not the woman's choice, she will need to continue to take medication throughout pregnancy. It should be remembered that as with the initial introduction of medication, as discussed on page 6, the choices of drug should never be presented as being either 'perfect' or 'harmful' as the 'perfect' drug may prove unsuitable and others may have to be tried. A woman's reluctance to take any medication during pregnancy, and particularly where its teratogenic potential has been highlighted, is understandable, but the risk should be put into perspective: the risk to the developing fetus from uncontrolled seizures in pregnancy resulting from sudden withdrawal from or non-adherence to AED medication is probably greater than the risk from continued exposure; the risk to the pregnant woman if she abruptly stops her medication includes the risk of prolonged seizures (status epilepticus) or, in rare instances, even sudden unexpected death (SUDEP). Recent reports from the Confidential Enquiries into Maternal Deaths in the UK have shown that there is concern about epilepsy and poor seizure control, which may well be as a result of non-adherence to AED medication.

If treatment is to continue during pregnancy, careful consideration must also be given to minimizing the risk of teratogenicity in the developing fetus. The risk is directly related to the number and type of AEDs the woman is taking: polytherapy carries a risk of 15–20%, while monotherapy carries a risk of about 4–6%. There is also a small differential effect between the AEDs. As the first data are emerging from epilepsy and pregnancy registers worldwide, an analysis of data from the UK Epilepsy and Pregnancy Register (Morrow et al, 2004) showed that although the overall risk remains low, women taking sodium valproate during pregnancy appear to have a significantly increased risk of having a child with major malformations (a rate of 5.9%) compared with those women taking carbamazepine or lamotrigine (rates of 2.3% and 2.1% respectively). A recent retrospective study of children born to mothers with epilepsy, undertook to assess the developmental, neuropsychological and dysmorphic features of children exposed to AEDs in utero, relative to children of women with epilepsy unexposed to AEDs (Adab et al 2004; Vinten et al 2004). Results showed that exposure to sodium valproate and frequent tonic–clonic seizures in pregnancy were both associated with a significantly lower verbal IQ, despite adjusting for other confounding factors. This is the first clinical evidence to suggest that frequent tonic–clonic seizures and exposure to sodium valproate have a similar effect. This therefore emphasizes that women with epilepsy need careful counselling about the individual risk–benefit profile of AED treatment before pregnancy. Women of childbearing potential should not be started on sodium valproate without specialist neurological advice. Sodium valproate is the antiepileptic drug of choice in women with certain types of epilepsy, such as generalized epilepsy with or without

myoclonus/photosensitivity; for partial epilepsy, sodium valproate should be used only in women resistant to other treatment.

As women with epilepsy are at higher risk than the general population of having a child with a neural tube defect, and particularly if they are taking sodium valproate or carbamazepine, a high dose (5 mg/day) of folic acid should be prescribed preconceptually and until at least the end of the first trimester.

Women with epilepsy may be concerned about the genetic risk of passing on their condition to their children. This is a complex issue. For most forms of epilepsy the risk is around 3% but it can be significantly higher in specific syndromes, and the advice of a consultant epileptologist or a clinical geneticist may be required.

KEY PRACTICE POINTS

- Women with epilepsy should be reassured that if they decide to have children, their pregnancies, although medically complicated, are likely to be uneventful and they are likely to deliver healthy babies.**
- Women with epilepsy should be offered, soon after diagnosis and well in advance of a pregnancy, comprehensive preconceptual counselling to enable them to make informed decisions about minimizing the risk factors for themselves and their baby.**
- Preconceptual issues include: planning a pregnancy, teratogenic risk of all AEDs, importance of seizure control and adherence to medication in pregnancy, introduction of high-dose folic acid before conception, and genetic counselling.**
- Preconceptual issues should be raised at every annual review in women of childbearing age.**
- Women should be referred to the local specialist epilepsy service for preconceptual counselling and to other sources of information (an epilepsy helpline or the UK Epilepsy and Pregnancy Register).**
- GPs should consider the possibility of pregnancy in all women of childbearing age at each review.**
- Women with epilepsy who are planning a pregnancy should be referred for review of diagnosis and treatment.**
- If a pregnancy is planned, it is possible that medication can be optimized prior to conception in terms of maximum seizure control and minimum risk to fetal development. Monotherapy at the lowest effective dose will minimize risk.**
- There is a small differential effect between the AEDs, in particular, recent studies suggest that in utero exposure to sodium valproate carries a higher risk than exposure to other AEDs.**
- Changes in type of antiepileptic medication should only be made on specialist advice and there should be no abrupt changes to or withdrawal from medication.**
- Importance of adherence to medication should be emphasized and explained.**
- High-dose (5 mg/day) folic acid supplementation is recommended preconceptually and for at least the first trimester.**

Management during pregnancy and postpartum

Up to 3–4 of every 1000 pregnancies occur in women with active epilepsy. The overwhelming majority of these will have an uneventful pregnancy and will deliver a healthy baby (92–96% compared with 98% in the general population). However, as already mentioned, these pregnancies are medically complicated and do require careful management. The GP needs to be aware of the following issues in the pregnant woman with epilepsy:

- effects of epilepsy and AEDs on the pregnancy;
- effects of pregnancy on AEDs and seizure control;
- effects of epilepsy, and particularly some types of seizures, on the developing fetus;
- effects of AEDs on the developing embryo/fetus.

Seizure control should be optimized throughout pregnancy, with seizure freedom being the aim; the importance of adherence to medication must be emphasized, but women should also be advised to protect themselves against becoming too tired and not getting enough rest and sleep. Ideally, a pregnancy will have been planned, allowing seizure control and medication to have been optimized preconceptually by a specialist. Even for the woman who presents with an unplanned pregnancy, who is possibly taking antiepileptic medication that significantly heightens her chances of having a malformed baby, there should be no abrupt withdrawal or changes to medication. Uncontrolled seizures in pregnancy resulting from sudden withdrawal from or non-adherence to antiepileptic medication may present a greater risk to the developing fetus than AED exposure. Also, organogenesis occurs at an early stage in pregnancy, often before the woman realizes she is pregnant.

Pregnant women with epilepsy should be jointly referred early for shared care with the nearest obstetric centre that offers high-resolution ultrasound scanning (screening for malformations is important in this population), and to the secondary epilepsy service. Ideally, an obstetrician who specializes in medically complicated pregnancies should be identified. If there is no shared service between these specialties, the GP will need to be proactive in managing the two sources of information to ensure that the woman receives consistent information and continuity of care.

There may be an increased risk of seizures in pregnancy and postpartum. Assessment of drug level changes in pregnancy is complex and these need to be interpreted on an individual basis by a specialist. Changes to drug dose should only be made on specialist advice.

A high dose of folic acid (5 mg/day) should be prescribed preconceptually and until at least the end of the first trimester.

Expectant mothers taking enzyme-inducing AEDs should be advised that to protect their

baby against haemorrhagic disease of the newborn, oral vitamin K (20 mg/day) is recommended from the 36th week of gestation until delivery, and their babies should be given intramuscular vitamin K (1 mg) at birth and 28 days post delivery.

Pregnant women are often concerned about how they will manage once their baby is born, and there are particular safety issues for some women with epilepsy. The mother may be better prepared for, and more confident in, caring for her baby if she has had an opportunity during the antenatal period to discuss which safety precautions may be helpful for her to consider. These precautions aim to minimize risk to the baby and mother but maximize opportunities for bonding. Where the mother has sudden, frequent or unpredictable seizures, the following safety measures are recommended: the mother feeds the baby whilst sitting on the floor, supported by cushions; changes the baby at floor level on a changing mat, which is safer than bathing the baby in water *unless* there is someone to assist her; safety gates (or playpen) may be helpful in preventing the mobile infant from wandering upstairs or close to a hazard such as the oven.

It is good practice to remind women to pack their medication in the bag that they will take with them on admission to hospital for delivery (if delivery is at night, the pharmacy may well be closed). It is also important to emphasize the need to continue to take their medication as usual during labour.

Women with epilepsy are often concerned about having a seizure during labour. Most will have uncomplicated vaginal deliveries, although the woman should ensure that the midwife and obstetrician are aware that she has epilepsy. However, in 2–4% of cases the stress and exertion of labour may increase the risk of seizures during labour or in the subsequent 24 hours. Women with epilepsy should always be delivered in an obstetric unit equipped with facilities for maternal and neonatal resuscitation.

AEDs are excreted in breast milk, but breast feeding (except in very rare cases) is safe, and it should be recommended if this is the mother's preferred choice as it may even help wean the baby from the higher levels of AEDs to which he/she was exposed in utero; however, mothers should watch for drowsiness in their infants. Women should be advised against extreme tiredness, which may exacerbate seizures. Their partner or another person managing the feeds at night may help protect against exhaustion.

GPs should undertake a postnatal *epilepsy review* of the mother 6 weeks after delivery, and it is good practice for the woman to be seen by a specialist 12 weeks after delivery. AED dose may have been increased in the later stages of pregnancy, and this may need to be gradually reduced postnatally, under specialist supervision.

KEY PRACTICE POINTS

- Pregnant women with epilepsy should be jointly referred to the nearest obstetric service with high-resolution ultrasound scanning, and to the local epilepsy service.**
- A well-planned pregnancy, with optimal seizure control, is the aim.***
- Changes in drug levels during pregnancy are complex and need to be interpreted and advised upon by a specialist on an individual basis. Medication should only be changed on specialist advice.**
- The woman should be informed antenatally of the safety precautions she may need to adopt in caring for her baby.**
- High-dose folic acid (5 mg/day) should be prescribed *prior to conception* until at least the end of the first trimester.**
- Vitamin K (20 mg/day) should be given to mothers on enzyme-inducing AEDs from the 36th week of gestation until delivery, and intramuscularly (1 mg) to babies at birth and 28 days after delivery.**
- Women with epilepsy should be reminded to take their medication with them when they go into hospital to have their baby and to continue to take this as usual during labour.**
- Breastfeeding is safe and is generally recommended.**
- GPs should undertake a postnatal *epilepsy review* at 6 weeks post delivery, and it is good practice for the woman also to be seen by a specialist 12 weeks after delivery.**



Checklist for completion of an eyewitness report

This checklist is based on *'How else can I help? – recording information about seizures'*, in the information on *'First Aid for Epilepsy'*, The National Society for Epilepsy website, www.epilepsynse.org.uk. (Reproduced with permission of the National Society for Epilepsy.)

- Keep a record of the dates and times that 'seizures' occur.
- Where was the person and what were they doing before the seizure?
- Did you notice any mood change, such as excitement, anxiety or anger?
- Did the person mention any unusual sensations, such as odd taste or smell?
- Did the seizure occur without warning?
- What drew your attention to the person having a seizure (e.g. a cry, a fall, or body movements such as eyes rolling or head turning)?
- Did the person lose consciousness or appear confused?
- Did the person change colour (e.g. become pale, flushed or 'blue')? If so, where (e.g. face, lips or hands)?
- Did the person's breathing alter (e.g. become noisy or difficult)?
- Did any part of their body stiffen, jerk or twitch? If so, which?
- Was there any incontinence?
- Did they bite their cheek or tongue?
- Did the person do anything unusual such as mumble, wander about, fumble with their clothes or any objects?
- How long did the 'seizure' last?
- How was the person after the 'seizure'?
- Did the person feel tired, need to sleep? If so, for how long?
- How long was it before the person was able to resume normal activities?
- Did you notice anything else?

References and further reading

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Sources of further information

Voluntary organizations

Epilepsy Action (British Epilepsy Association)

New Anstey House, Gate Way Drive, Yeadon, Leeds LS19 7XY

Tel: 0113 210 8800

Helpline: 0808 800 5050

E-mail: helpline@epilepsy.org.uk

Website: www.epilepsy.org.uk

Epilepsy Scotland

48 Govan Road, Glasgow G51 1JL

Tel: 0141 427 4911

Helpline: 0808 800 2200

E-mail: enquiries@epilepsyscotland.org.uk

Website: www.epilepsyscotland.org.uk

The National Society for Epilepsy

Chesham Lane, Chalfont St Peter, Buckinghamshire SL9 0RJ

Tel: 01494 601300

Helpline: 01494 601400

Website: www.epilepsynse.org.uk

Professional website: www.e-epilepsy.org.uk – this website is for individuals with a professional interest in epilepsy; the information is relevant to GPs and they can e-mail questions directly to the medical experts at NSE.

UK Epilepsy and Pregnancy Register

c/o Dr JI Morrow, Department of Neurology, Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA

Helpline: 0800 389 1248

Website: www.epilepsyandpregnancy.co.uk

DVLA

Swansea, SA99 1BN

Tel: 0870 240 0009 (general enquiries); 0870 600 0301 (medical adviser)

Website: www.dvla.gov.uk

Epilepsy Bereaved

PO Box 112, Wantage, Oxon OX12 8XT

Tel: 01235 772850

Bereavement contact line: 01235 772852

Website: www.sudep.org

This organization does not offer a counselling service, but is pleased to help and support bereaved relatives through its bereavement contact line above.

Guidelines

Scottish Intercollegiate Guidelines Network (SIGN). The Management of Pregnancy in Women with Epilepsy. A Clinical Practice Guideline for Professionals Involved in Maternity Care. See: www.show.scot.nhs.uk/sign/guidelines

Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of epilepsy in adults. Guideline 70, April 2003. See: www.show.scot.nhs.uk/sign/guidelines

In March 2004, NICE issued guidance to the NHS in England and Wales on the use of newer antiepileptic medication in children and adults. See: www.nice.org.uk/Docref.asp?d=110323

NICE will publish a guideline on the management of epilepsy in Autumn 2004.

The new GMS contract and developing roles for GPs

The new GMS contract for GPs came into effect in April 2004, and for the first time these include quality markers for specific disease areas or medical conditions, against which GPs can earn points that will bring extra income for the additional services provided. Epilepsy is included with four quality markers: produce a register of those patients who are receiving drug treatment for epilepsy; undertake a medication review of patients with epilepsy aged over 16 years; record seizure frequency; aim to achieve seizure freedom in at least 70% of patients. See: www.bma.org.uk

Epilepsy is also included in the Competencies Framework for GPs, developed by NatPaCT (part of the NHS Modernisation Agency). NatPaCT recommends to PCTs the kind of services they should be offering through the Competency Framework, although the Framework is not prescriptive. See: www.natpact.nhs.uk

The developing role of GPs with a special interest (GPwSI) is also potentially significant for improved epilepsy care. The GPwSI programme aims to develop specialist knowledge and expertise among GPs in a particular therapeutic area to enable them to provide more specialist services within the community they serve; they would be able to take referrals from colleagues or provide enhanced services, thus allowing many patients faster access to specialist treatment. See: www.gpws.org