The management of epilepsy in pregnancy

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Introduction

Epilepsy is the most commonly encountered serious neurological problem faced by obstetricians, gynaecologists and primary care physicians. Its importance lies in the fact that the majority of women with epilepsy (WWE) will need to continue antiepileptic drugs (AEDs) prior to and during pregnancy. The disease and these medications may significantly impact on reproductive function, contraceptive choice and efficacy. During pregnancy, the clinician faces the dual challenge of maintaining seizure control, yet minimising teratogenic risk. The purpose of this review is to provide an update on management of WWE prior to and during pregnancy. In particular, pre-pregnancy and contraceptive recommendations will be addressed, and updated information provided regarding the teratogenicity of AEDs, including the newer AEDs. This overview will also examine the role of therapeutic drug monitoring (TDM) in pregnancy, obstetric complications facing WWE and recommendations to optimise antenatal, intrapartum and postpartum care.

Preconception care

Specific considerations for women of reproductive age with epilepsy include consideration of sexuality and reproductive function and avoiding unplanned pregnancy with reliable contraception. When pregnancy is planned, AED medication should be optimised and adequate folic acid supplementation instituted. Awareness of these issues remain poor; despite a national education programme, a recent study found that only 46% of WWE recalled being provided with information on the interactions between AEDs and contraceptives, 63% on the need to plan pregnancy and only 56% on the need for folic acid supplementation.1

Reproductive function and fertility in WWE

Increased rates of sexual dysfunction are reported among both men and WWE. This may arise from both neuroendocrine disturbances related to seizure activity, as well as the alteration of endogenous sex steroid metabolism in the presence of enzyme-inducing AEDs.2 Hypothalamic amenorrhoea, hyperprolactinemia and premature menopause are over-represented among WWE, thought partly because of interference with normal hypothalamic and pituitary function by temperolimbic discharges commonly involved in epilepsy.3 An increase in anovulatory cycles and polycystic ovarian syndrome (PCOS) has also been observed in WWE.3,4 While this may partly relate to disturbance of the Hypothalamic-pituitary-adrenal (HPA) axis, AEDs may also play a role.4 Enzyme-inducing (EI) AEDs increase serum sex hormone binding globulin (SHBG) levels, resulting in decreased levels of biologically active estradiol and testosterone. In addition, valproic acid (VPA) is associated with an increased rate of hyperandrogenism, ovulatory dysfunction and PCOS, particularly among
young (<26 years) women, suggesting a direct effect on ovarian androgen production. These observations are consistent with the findings that fertility is lower among patients with epilepsy, although, a recent Scandinavian population-based cohort study suggests the impact is relatively modest. The birth rate was lower in WWE than the population without epilepsy, (hazard ratio 0.83, 95% CI 0.83–0.93). A follow-up study did not find any significant differences between treated and untreated women, suggesting that while women may have a mild reduction in fertility associated with epilepsy, the use of AEDs does not significantly impact further.

Contraception
The efficacy of hormonal contraception may be reduced by EI AEDs, such as phenobarbital, primidone, phenytoin, carbamazepine, oxcarbazepine, felbamate and topiramate, all of which – by inducing hepatic enzymes in the cytochrome P-450 system – increase clearance of contraceptive steroids. In addition, EIAEDs increase the level of SHBG, which in turn decreases the levels of freely circulating progestins. Hormonal contraceptive efficacy is not affected by non enzyme-inducing AEDs, such as including VPA, zonisamide, benzodiazepines, gabapentin, levetiracetam, pregabalin, tiagabine and vigabatrin. Lamotrigine has been previously thought not to impact on contraceptive efficacy, a recent study has demonstrated a significant decrease in plasma levonorgestrel concentration and some reduction in hypothalamic-pituitary suppression, albeit without evidence of breakthrough ovulation.

The accelerated metabolism of estrogens and progestogens in the combined oral contraceptive pill (COCP) means that plasma concentrations may fall below the levels required for inhibition of ovulation. Contraceptive alternatives, such as depo medroxyprogesterone acetate (DMPA), a levonorgestrel releasing intrauterine contraceptive device (Mirena) or barrier methods may be considered preferable for WWE taking EIAEDs. Where COCP use is necessary, a higher estrogen dose COCP (e.g. 50 μg of ethinyl estradiol) has traditionally been recommended. Nevertheless, it is the increase in progestin dose that is necessary for ovulation suppression; hence, the recommendation to increase both estrogen and progestin (for example, by taking 2 Microgynon 30 tablets daily). A residual risk of breakthrough pregnancy remains, because the extent of enzyme induction varies among women. To improve contraceptive efficacy further, tricyclic the pill is recommended (i.e. three cycles of hormonal contraception without a break) followed by a shorter pill free interval (4 days). Extended cycle regimes such as this more reliably inhibit ovulation by preventing follicular development during the pill-free period, and may further improve contraceptive efficacy by uninterrupted thickening of cervical mucus and modulation of the endometrium. The reduction in circulating levels of levonorgestrel among patients receiving EIAEDs means that the low dose (or mini-pill) progestin-only pill is not recommended for these patients.

With regard to the effect of COCPs on AED levels, recent studies suggest that administration of COCPs increase metabolism of lamotrigine (via increased glucuronidation), reducing levels by approximately 50%. This has been associated with a significant worsening of seizure control. An increase in lamotrigine dose is therefore required when commencing the COCP with appropriate reduction upon cessation. The benefit of continuous ( uninterrupted) oral contraceptive use among lamotrigine users is thus two-fold; to improve contraceptive efficacy and maintain stable plasma lamotrigine concentrations. The metabolism of oxcarbazepine, like lamotrigine, is via glucuronidation, so a similar effect on oxcarbazepine levels would be expected and warrants further exploration.

A small study of women using levonorgestrel implants (Norgestimate) for contraception reported lower levonorgestrel levels among women using phenytoin compared with control women. Two subsequent breakthrough pregnancies were associated with low plasma levonorgestrel concentrations around the time of conception suggesting that perinatal levonorgestrel is ineffective among patients receiving EIAEDs. Several case reports have followed, resulting in the recommendation that this form of contraception be avoided among women taking EIAEDs. The contraceptive efficacy of the etonogestrel implant (Implanon) has likewise been reported to be reduced among WWE using EIAEDs. In the first 3 years of marketing in Australia, 218 unplanned pregnancies were reported in the 204,486 subsidised insertions, giving an approximate failure rate of 1:1000. Eight of these Implanon failures were in association with EIAEDs with seven of the eight women using carbamazepine. Likewise, 39 unintended pregnancies were reported after 17 months of Implanon use in France; 2 in association with hepatic EI medication. The product information recommends the use of an additional barrier method of contraception in WWE taking hepatic EIAEDs.

Despite the disappointing results from subcutaneous progesterin implants, administration of high dose DMPA continues to provide effective contraception in women taking hepatic EIAEDs. That DMPA has been shown to reduce seizure frequency in some WWE means that DMPA may be a preferred contraceptive method. The disadvantages of DMPA as a long term contraceptive include delayed return to fertility, irregular bleeding and adverse effects on bone mineral density, particularly among adolescents who may not achieve peak bone density. The United States FDA recommends that the benefits and risks be discussed with women prior to commencement of DMPA and reassessed.
after 2 years of continuous use. While some authorities suggest administering DMPA every 10, rather than 12, weeks to women receiving EIAEDs, DMPA is subject to 100% first pass hepatic metabolism, such that the presence of enzyme inducers cannot accelerate metabolism further.

The levonorgestrel-releasing intrauterine device (Mirena) is a highly effective form of contraception as the progesterone effect is locally mediated and less affected by the EIAEDs. Given that it is both reversible and highly effective, with an estimated failure rate of 1% among these women, a levonorgestrel-releasing IUCD has been suggested as the first line contraceptive choice for WWE using EIAEDs or lamotrigine. With appropriate pre-insertion counselling and advice, Mirena is gaining increasing acceptance for nulliparous women, including young women and adolescents.

Optimising AEDs for pregnancy

There are widespread concerns about the teratogenic risks posed by AEDs, but any potential benefit of ceasing or changing medication must be weighed against a risk of increased seizure frequency, with the attendant risk to the patient, her fetus and possibly other children. Women with well controlled epilepsy (e.g. seizure free for 2–5 years) may be eligible to stop or reduce their medication prior to pregnancy, and women taking more than one AED may consider a trial of monotherapy. The risk of seizure relapse appears to be lower in the presence of a normal neurological examination/IQ, normal EEG and normal neuroimaging. However, certain syndromes that are easily controlled with medication have a high rate of relapse off medication, such as juvenile myoclonic epilepsy (JME). The risk of seizure relapse is highest soon after drug withdrawal or dose reduction, and it is preferable that pregnancy is deferred until stabilisation is achieved. During this transition period, WWE should be particularly wary of lifestyle exacerbants, such as sleep deprivation, stress and alcohol consumption. They should be aware of the implications for their driving license in the event of a seizure. The complexity of this decision-making underscores the value of WWE consulting both their neurologist and obstetrician when contemplating a pregnancy.

Teratogenicity of epilepsy and AEDs

The risk of congenital malformation is higher in WWE. In an effort to better quantify the risk of treated versus untreated epilepsy, a Finnish population-based study has compared the risk of major malformation in WWE, with and without treatment. This study confirmed that major congenital malformations were more common among women on AEDs (4.6%) than among untreated patients (2.8%), OR 1.7 (95% CI 1.05–2.81). Given the differing patterns of both seizure severity and type between treated and untreated patients, the pathogenesis of fetal malformations is likely to be multifactorial. In addition to the direct effect of AEDs, there may be contribution from toxic AED metabolites, reduced folate availability, hypoxic injury associated with seizures and genetic predisposition.

While specific dysmorphic phenotypes have been described with many of the commonly used AEDs, it is the incidence of major congenital malformation that causes most concern. The precision of risk estimation with any individual AED is imperfect as there is a paucity of controlled data, and an uncertain impact of potential confounders, such as type of epilepsy, seizure frequency, family history of birth defects, socio-economic factors, nutrition and exposure to additional teratogens. The development of AED registries addresses many of these problems by prospectively enrolling large numbers of WWE taking AEDs at the start of pregnancy with systematic follow up of pregnancy outcomes. These registries are one of three types; independent academic registries, pharmaceutical drug registries and population-based registries. The independent registries include; the European and International Registry of Antiepileptic Drugs and Pregnancy (EURAP), originally established in Europe in 1999 and later extended to include 30 countries in Europe, Asia, Oceania and South America, the North American Antiepileptic Drug Pregnancy Registry (established in 1997), the United Kingdom Epilepsy and Pregnancy Group (established in 1996), and the Australia Pregnancy Registry of Women taking Anti-epileptic Drugs (established in 1999). Two pharmaceutical registries include the GlaxoSmithKline’s International Lamotrigine Pregnancy Registry, and the recently launched UCB Antiepileptic drugs (AED) registry [formally the Keppra (levetiracetam) registry]. The Swedish and Finnish national registries provide information on the prevalence of birth defects linked to antenatal or national prescription data identifying WWE.

While AED registries provide the most robust data on teratogenic risk when compared with the cohort and case control studies that preceded them, their individual strengths and limitations need to be appreciated. National registries provide the best population-based data, but detail on epilepsy type and drug dosing is often limited, and incidence data is limited by lack of information on termination of pregnancies. The independent academic registries suffer from methodological differences between registries, incomplete information regarding dosages and confounding variables and incomplete enrolment (for example, 30% in the UK Registry, which has among the highest participation rates). It is estimated that approximately 500 monotherapies are required to confidently identify differences in major congenital malformations between AEDs. Larger numbers again are required to examine for a dose-response relationship and to adjust for confounding variables. Notwithstanding these limitations, these registries provide
the best available estimates of teratogenic risk for the common monotherapies. The quality of information will only improve with time, and it is recommended that all WWE be registered with their local Anti-Epileptic Drug Registry.\textsuperscript{36} The most recent published data for the common AEDs from the above mentioned registries are presented in Table 1. This data reflects the considerable experience and safety with carbamazepine as a single agent, although the accumulating data on lamotrigine also appears reassuring. These results are similar to the findings of a meta-analysis published in 2008 including registry and cohort data up until May 2007.\textsuperscript{47} The incidence (95% confidence intervals) of malformations for monotherapy was as follows: carbamazepine 4.6% (3.5–5.8%), lamotrigine 2.9% (2–3.8%), phenobarbital 4.9% (3.2–6.6%), phenytoin 7.4% (3.6–11.1%) and valproate 10.7% (8.2–13.2%). As a single agent, VPA consistently has the highest rate of malformations, and several investigators have reported a dose-response relationship between valproate and major malformation.\textsuperscript{27,48–50}

The safety data on the newer AEDs is limited. While the overall incidence of major congenital malformation with lamotrigine appears acceptable, it remains uncertain whether lamotrigine is associated with an increased risk of facial clefting.\textsuperscript{42,51,52} There have been small case series suggesting an increase in low birthweight among infants of WWE receiving topiramate\textsuperscript{53} and levetiracetam,\textsuperscript{54} but these findings warrant validation in larger studies. Similarly, malformations have been reported in 6/248 (2.4%) of patients receiving oxcarbazepine in pregnancy,\textsuperscript{55} and 2/44 (4.5%) of patients receiving gabapentin.\textsuperscript{56} Vigabatrin is associated with acquired visual field defects and its safety is not established in pregnancy.\textsuperscript{57} The risk of malformation with polytherapy is higher than with monotherapy. While it is difficult to determine individual risks for all possible polytherapy combinations, the meta-analysis of Meador \textit{et al}.\textsuperscript{47} reported that the rate of total congenital malformations was significantly higher for polytherapy (9.84%; 95% CI = 7.82, 11.87) than for monotherapy (5.3%; 95% CI = 3.51, 7.09).

In summary, the risk of congenital malformation is higher among treated WWE than untreated women and those using polytherapy rather than monotherapy. As a single agent, VPA (particularly in doses >1100 mg/day) appears to be associated with the highest risk and this is further amplified when combined with other AEDs.\textsuperscript{57} In the face of this data, modification of AEDs pre-conception may be indicated to minimise teratogenic risk. To further minimise this risk, high dose (5 mg) folic acid is generally recommended for at least 1 month pre-conceptually and throughout the first trimester.\textsuperscript{26} EIAEDs and valproate are known to interfere with folic acid metabolism,\textsuperscript{58} and Kjaer \textit{et al}. reported fewer congenital malformations in women taking AEDs with folic acid, compared to those not given additional supplementation.\textsuperscript{59}

### Neurocognitive effects

In addition to structural malformations associated with AEDs, there has been increasing concern regarding the...
The most significant effects were seen for polytherapy and had significantly lower scores than those infants unexposed. A mean age of 15 months. Infants of mothers taking AEDs mental quotients of 395 infants of mothers with epilepsy at have reported an increase in educational requirements,61,62 Thomas et al. has recently reported on 1882 WWE where seizure complicating a vaso-vagal faint.

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to alternate diagnoses, such as eclampsia, a primary neuro-

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Taken collectively, the data consistently demonstrates stronger associations between VPA and both major malfor-
mations and neurocognitive effects, but it must be emphas-
ised that data on neurocognitive outcomes is relatively recent, methodologically challenging and further prospec-
tive studies are essential. Large numbers will be needed
before there is a reasonable probability of separating the
effects of the various AEDs from confounders such as
seizure frequency, type of epilepsy, genetic factors and
parental cognitive function.

Pregnancy care

In the antenatal period, obstetricians caring for WWE need to consider the likely impact of pregnancy on seizure frequency, the potential impact of epilepsy on obstetric outcomes, the role of TDM of AEDs, surveillance for congenital malformations and the place of vitamin K supplementation. In women who present during pregnancy with their first seizure, consideration should also be given to alternate diagnoses, such as eclampsia, a primary neuro-

logical event, metabolic disturbance or drug toxicity or a
seizure complicating a vaso-vagal faint.

The behaviour of epilepsy in pregnancy,
and its effect on pregnancy outcomes

Until recently, there was limited prospective data on sei-

ure frequency during pregnancy. The EURAP registry has recently reported on 1882 WWE where seizure control and treatment was prospectively recorded. 58% of participants were seizure free during pregnancy. When first trimester seizure activity was used a reference, 64% had no change in the second and third trimester, 16% improved, while only 17% deteriorated.67 In the absence of information on pre-pregnancy seizure control, this study cannot fully address the impact of pregnancy on epilepsy, but it suggests it is probably modest. One notable exception is that tonic-clonic seizures occurred more frequently among women taking oxcarbazepine monother-

apy.67 The increased clearance of lamotrigine and oxcarbazepine observed with COCP use is also observed in pregnancy,16,68 and suggests these WWE may be partic-

ularly vulnerable to breakthrough seizures with falling AED levels.

The Australian Register of AEDs in pregnancy also found that pregnancy had little impact on seizure frequency among treated women. Seizures occurred during pregnancy in 418/841 (49.7%) of AED-treated pregnancies. A 12 month ‘seizure-free’ period prior to pregnancy was asso-
ciated with a 50–70% reduction in seizure risk during preg-
nancy.69 If seizure control deteriorates in pregnancy, potential contributors include: decreased medication com-
pliance because of concern about teratogenesis; decreased
derg absorption because of nausea and vomiting, impaired
leep and decreased drug levels because of both increased
volume of distribution in pregnancy and increased drug
metabolism.

While the fetus is relatively resistant to short hypoxic episo-
des, prolonged convulsive seizures may result in
sustained fetal hypoxia. Protecting the fetus from the con-
sequences of frequent or sustained seizures is a compelling
argument for maintaining AED use in pregnant WWE. This notwithstanding, the EURAP registry has provided some reassuring data regarding the impact of seizures on pregnancy outcome. Among 1956 WWE, 30 stillbirths (1.5%) were recorded, which is somewhat higher than the
0.5% that might be expected in a non-selected population. Half of these were among the 943 (1.5%) women with
seizures and the other 15 stillbirths occurred in the 1013 (1.5%) who were seizure free.67 Status epilepticus compi-
lated 36/1956 (1.8%) pregnancies. Thirty-four of these
pregnancies resulted in a livebirth, one ended with a
miscarriage and one with stillbirth. This suggests that status epilepticus may not have as poor an outcome in pregnancy as previously believed. This apparent improvement may be a consequence of both better data collection and better
treatment of status epilepticus, including a lowered thresh-
old for delivery. Overall, this data suggests that the rate of
fetal loss because of epilepsy (or AED treatment) is low,
but more information on longer-term infant outcome would be of value. The advent of large prospective regis-
tries should facilitate better obstetric data collection,
thereby improving precision in the estimate of the true fetal and obstetric risk.

The impact of epilepsy on other obstetric outcomes appears modest. A prospective cohort of 414 WWE revealed increased rates of pregnancy-induced hypertension and induction of labour, but no other increased obstetric morbidities. A single centre prospective study from Finland of 179 pregnancies of WWE and 24 778 controls found no significant differences in the rate of pre-eclampsia, preterm delivery, caesarean section or perinatal mortality. The number of small for gestational age infants (defined as less than the 10th centile for gestational age) was higher (17.3% versus 9.3% in control pregnancies), as was the rate of neonatal unit admission (13.4% versus 7.4%). A Swedish study of 1207 women taking AEDs in pregnancy compared with 559 491 controls found a significant increase in the incidence of pre-eclampsia (OR 1.66, 95% CI 1.43–1.89), and caesarean section (OR 1.64, 95% CI 1.32–2.08). The observed increase in postpartum bleeding and neonatal respiratory distress may have been partly attributable to this latter observation. An Israeli study of 220 WWE also observed an increase in the caesarean section rate. This higher incidence of caesarean delivery among WWE is likely to be multifactorial, but may be partly mediated by the observed increase in fetal growth restriction and hypertensive disorders of pregnancy. In the future, the linking of obstetric outcomes to AED registries should generate more precise estimates of these risks.

TDM in pregnancy
Antiepileptic drug pharmacokinetics may be significantly altered in pregnancy by changes in body weight and effects on drug absorption, protein binding, metabolism and excretion. Serum concentrations of older AEDs, such as phenobarbitone, primidone, carbamazepine, phenytoin and VPA have all been shown to be decreased in pregnancy. Some of this reduction is related to the reduction in serum protein in pregnancy, meaning that the total drug concentration is lower, but the unbound (active) concentration is stable. This is particularly relevant for highly protein bound drugs, such as VPA and phenytoin. As noted above, a clinically significant reduction in plasma concentrations of both lamotrigine and oxcarbazepine occurs in pregnancy, as well as levetiracetam. There is a paucity of data on the pharmacokinetics of the newer AEDs, such as gabapentin, topiramate and zonisamide.

In WWE, the goal of therapy is to maintain seizure control using the lowest effective AED dose. The International League Against Epilepsy position paper recommends that drug concentrations be determined during pregnancy. It is recommended that – prior to pregnancy – an individual ‘therapeutic level’ during a period of optimal seizure control should be determined, which can then serve as a ‘target level’ for pregnancy. Among patients with good control, serum concentration should be performed each trimester, but more frequent (for example, monthly) levels may be required in patients with complicated epilepsy, breakthrough seizures, significant side effects and those WWE requiring lamotrigine and oxcarbazepine where highly variable and more clinically significant fluctuations in drug concentration have been observed.

Surveillance for birth defects
In WWE, especially those taking AEDs, an 11–13 weeks ultrasound examination should be offered. Acrania (the precursor of anencephaly) should be recognised at this gestation, and an increased nuchal translucency is also a useful screening test for cardiac and other structural defects. At midtrimester, an expert morphological assessment should be performed. Note should be made on the referral of the history of epilepsy, and the medication regimen so that a targeted assessment, particularly of the neural axis, heart and face can be performed. Where there is adequate provision of expert ultrasound services, the place of adjuvant screening for neural tube defects with midtrimester serum alpha-fetoprotein is limited. While serum screening will detect virtually all pregnancies with anencephaly, the sensitivity for detecting neural tube defects overall is only 65%, rising to 86% if gestational age is confirmed on ultrasound. In contrast, detection rates with high level ultrasound for open NTDs are from 97% to 100%, with those undetected being covered defects, less likely to have the characteristic ‘head signs’.

Vitamin K supplementation
It has been previously proposed that the use of enzyme-inducing AEDs may induce fetal hepatic enzyme activity culminating in vitamin K deficiency and increased risk of neonatal bleeding, and that vitamin K should be administered to such women in late pregnancy to minimise this risk. Several case control studies have challenged this recommendation after observing no increase in bleeding complications between neonates born to WWE receiving enzyme-inducing AEDs and healthy controls. In the largest study, however, the authors acknowledged the following caveats; these findings could not be generalised to preterm infants, all neonates in their study were administered Vitamin K and they acknowledged the study was underpowered to detect a small, but clinically significant increase in neonatal bleeding. Nevertheless, the findings of these studies have formed the basis of some consensus statements (for example, the NICE guidelines) that no longer recommend supplemental vitamin K for WWE receiving enzyme-inducing AEDs in late pregnancy, but just
administration of konakion (or phytomedanione) to the neonate.83

**Intrapartum care of WWE**

Labour and delivery is a relatively high risk time for seizure recurrence. The reasons for this are multifactorial including poor bioavailability and compliance with AEDs, sleep deprivation, anxiety and hyperventilation in labour. The EURAP registry reported seizures occurring in 60/1956 (3.5%) of epileptic women in labour.67 Although the presence of seizures occurring earlier in pregnancy was associated with seizures in labour (OR 4.8; 95% CI 2.3–10.0), a significant minority (14/60) had been seizure free for the entire pregnancy. All centres delivering obstetric care should therefore be mindful of the increased risk of seizure in labour, and manage WWE accordingly14,83,84 (Table 2).

**Postpartum care of WWE**

Maternal plasma levels of AEDs may fluctuate up until the eighth postpartum week and monitoring of plasma AED levels may be required. If doses have been increased during pregnancy, toxicity may occur and AED requirement is likely to fall in the puerperium. Lamotrigine and oxcarbazepine doses in particular may need to be reduced postpartum.

Most AEDs are compatible with breast feeding. The optimal method of estimating drug exposure is to measure the milk drug concentration and multiply it by the estimated daily intake. Typically, a value ≤10% of the weight-based therapeutic drug dose is considered safe. The estimated levels for carbamazepine, phenytoin and VPA are 3–5% of therapeutic dose and are considered safe.85 Estimates for lamotrigine and levetiracetam are approximately 10%, and gabapentin approximately 12%.85,86 The product information for these drugs recommends breast feeding only if the benefits outweigh the risks; further data is needed to establish the safety of these newer AEDs.

During their postnatal stay, WWE and all their maternity care providers should be aware of the risk of postpartum seizures, particularly in the setting of sleep deprivation. Ensuring such women get adequate sleep, and attention to medication compliance is of the utmost importance. Hospital staff should be particularly vigilant of women feeding alone in a single room at night. The woman’s neurologist and family doctor should be notified of delivery, and the predetermined regimen for AED medication and contraception in the puerperium instituted.

Upon discharge, WWE will be anxious about the prospect of having a seizure whilst caring for a baby at home alone. Although the risk to the infant from maternal seizures is generally low, women with JME are a particular concern, since myoclonic jerks tend to be more frequent in the early morning, often around the time of infant waking.14,87 WWE should be given advice regarding minimising the risk of seizures at home. This involves reinforcing the importance of medication compliance, and attention given to adequate sleep. The latter may be accomplished by expressing breast milk so that their partner can give the night feed. To minimise the risk of harm if a seizure occurs, changing or feeding the baby on the floor is recommended, the use of baby slings should be avoided, stair climbing should be minimised where possible and bathing the baby should be avoided when alone.14,87 The importance of adequate postnatal social supports cannot be over emphasised.

**Conclusion**

Most WWE will have a successful pregnancy, but pre-pregnancy counselling is necessary to optimise maternal and infant outcome. This allows for appropriate contraceptive planning, administration of high dose folic acid, and adjustment of medication to minimise teratogenic risk while maintaining seizure control. During pregnancy, prenatal detection of many structural malformations should be achievable with high quality ultrasound, yet an increased risk of undetectable malformation, including impaired neurocognitive development, remains. Prospective registration of all patients on AEDs will improve the precision of these risk estimates in the future. Increased surveillance for obstetric complications during pregnancy is necessary, as is appropriate TDM. The intrapartum and postpartum period is associated with an increased risk of seizure frequency, and all hospitals delivering obstetric care should have guidelines on how to minimise the risk of seizure and a protocol for their acute management. A multidisciplinary approach is necessary to
provide adequate support with postnatal care and discharge planning.

**Contribution to authorship**
All three authors have contributed to this review, with SW, MP and SB all involved in the final drafting of the manuscript.

**References**

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