Epilepsy in Pregnancy Management Guideline

N.B. Staff should be discouraged from printing this document. This is to avoid the risk of out of date printed versions of the document. The Intranet should be referred to for the current version of the document.
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Introduction

Background: Epilepsy affects approximately 350,000 people in the UK, between 30% and 40% of these are women of childbearing age¹. In Wales epilepsy is the commonest neurological condition with an estimated 20,000 – 30,000 people with active epilepsy². Epilepsy is associated with an increased risk of premature death due to accidents resulting from seizures, suicide, status epilepticus and unexpected deaths³.

Aims

To provide information to the healthcare staff about the services available in the Health Board to the women with epilepsy, how to access these, a guidance to the care in antenatal period and what to do in an emergency, in order to improve the care these women receive in their pregnancy

Objectives

Clarity in decision making for women with epilepsy during pregnancy

Scope

This document relates to all maternity staff and women with epilepsy in pregnancy

Pregnancy and Epilepsy

Effects of Pregnancy on Epilepsy

Seizure frequency increases during pregnancy in between a quarter and a third of women⁴ due to a number of factors including changes in pharmacokinetics of Anti Epileptic Drugs (AEDs) and poor adherence to treatment because of concerns about adverse effects on the fetus. Risks to the woman of injury and rarely, death in seizure remain in pregnancy⁷.

The recent MBRRACE report (2009-12) reported 17 maternal deaths due to epilepsy, 12 of which were from sudden unexpected death in epilepsy (SUDEP) and 2 cases resulted from drowning⁸. The higher than expected maternal deaths in UK may be related to non compliance with medication. This emphasises the importance
of pre-conceptual counselling in informing women of the risks of stopping AEDs.
Pregnancy is associated with pharmacokinetic changes including an increase in volume of distribution, an increase in drug metabolism through hepatic microsomal enzyme induction, a reduction in serum albumin concentration and an increase in renal clearance. There is a tendency for plasma levels of AEDs especially Lamotrigine, to fall in pregnancy but there is no evidence to support routine increase of AED doses. It is important to monitor seizure control closely.

There is no evidence of increased risks of obstetric complications in relation to pre-eclampsia, preterm delivery or placental abruption.

**Risks to the fetus from maternal epilepsy**

Tonic clonic seizures increase the pressure in the pregnant uterus and lead to transient changes in CTG and may also lead to trauma if the woman falls. Tonic clonic seizures can rarely result in lactic acidosis leading to fetal hypoxaemia. Reassuringly, recent reports suggest that the number of stillbirths in adequately treated women with epilepsy is similar to the background population.

Women should be made aware of the risks of uncontrolled seizures both to themselves and to the fetus and therefore the importance of compliance with medication.

**Risks to the fetus from AEDs**

Major and minor malformations occur more commonly in infants exposed to AEDs during pregnancy. The overall risk of major fetal malformations increases 2-3 fold in women taking AED, compared to a background risk of 1-2%. Polytherapy, particularly with certain combination of drugs, carries a much higher risk (up to 24% in women taking 4 AEDs).

The most common major malformations associated with AEDs is Neural Tube Defect (NTD), (Valproate 3%, Carbamezapine 1%), or facial clefts, congenital heart anomalies. The incidence of epicanthic folds and digital hypoplasia is also increased with AED therapy.

“Fetal Anticonvulsant syndrome” comprising typical dysmorphic craniofacial appearances and a variety of musculoskeletal abnormalities have been described in association with AED treatment in pregnancy. Although individual drugs have been associated with specific patterns, there is overlap between them and genetic factors may influence susceptibility.
<table>
<thead>
<tr>
<th>Drug</th>
<th>NTD</th>
<th>Facial cleft</th>
<th>Cardiac</th>
<th>Hypospadias &amp; GUT</th>
<th>GIT</th>
<th>Skeletal</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamezepine</td>
<td>0.2%</td>
<td>0.4%</td>
<td>0.7%</td>
<td>0.2%</td>
<td>0.2%</td>
<td>0.3%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Valproate</td>
<td>1%</td>
<td>1.5%</td>
<td>0.7%</td>
<td>1.3%</td>
<td>0.3%</td>
<td>1.1%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>0.2%</td>
<td>0.2%</td>
<td>0.6%</td>
<td>0.9%</td>
<td>0.5%</td>
<td>0.3%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>0</td>
<td>1.2%</td>
<td>1.2%</td>
<td>0</td>
<td>1.2%</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>


Whether AEDs taken during pregnancy can affect the child’s intellectual development is uncertain but a recent review from the MHRA (2015) reported that children exposed in utero to sodium valproate were at high risk (30-40%) of serious developmental disorders and/or congenital malformation (approximately 10%).

At present there is insufficient evidence on which to base advice about risks of most of the newer AEDs (Gabapentin, levetiracetam, tiagabine, topiramate, vigabactrin) in pregnancy. Current data on Lamotrigine show a malformation rate of 3%.

Where possible, epilepsy treatment should be reviewed before becoming pregnant. The effects of AEDs and risks of seizures should be explained.

- If the woman’s epilepsy is in remission, the risk of recurrent seizures is low and the woman is aware of the consequences of recurrent seizures, consideration may be given to reduction or withdrawal of AEDs prior to conception.
- If possible the woman should conceive on the lowest effective dose of AEDs appropriate for her epilepsy syndrome. If she is already pregnant and has good seizure control there is no benefit in changing the dose.
- Any woman who has had a child with AED related malformation should be reviewed by an epilepsy specialist before becoming pregnant again.
Risk of inheritance

Genetics of most epilepsies are complex with multiple genes involved and interaction of environmental factors. The risk of epilepsy in the offspring is higher with idiopathic than with symptomatic epilepsies.

Pre conception counselling:

Epilepsy is common in women of child bearing age and exposure to anti epileptic drugs (AEDs) occurs in approximately 1 in 150 pregnancies. It is important that the primary care giver- GP, Epilepsy Specialist Nurse, Neurologist be alert to the possibility of conception and discuss this with the women.(Harden, Hoop et al, 2009. National Institute for Health and Care Excellence, 2012.)

In those not planning a pregnancy, or in those who are being investigated or seizure control is not satisfactory, effective contraception should be prescribed.

Subjects to discuss in pre pregnancy counselling of women with epilepsy include:

- Women with epilepsy should be reassured that most will have a normal pregnancy and delivery.
- Genetic counselling regarding risk of inheriting epilepsy is low in most types of epilepsy.
- Risk of congenital anomalies associated with AEDs.
- Drug treatment – monotherapy is preferable at the lowest effective dosage. Good compliance with treatment is essential. Women should be informed of the potential risks as a result of stopping AED medication suddenly. Routine monitoring of AED levels in pregnancy is not recommended however where seizure control is poor, monitoring AED levels (particularly levels of lamotrigine and phenytoin) maybe useful when making dose adjustments (NICE 2012).
- Folic acid – 5mg daily should be taken from 3 months before conception to the end of the first trimester to reduce the risk of neural tube defects (NICE 2004)
- Antenatal screening tests – as for the general population of pregnant women - ultrasound can detect most neural tube defects
- Expected course of epilepsy and risk of seizures – the frequency of seizures usually remains unchanged as prior to
pregnancy. Drug doses may need to be increased in some women to maintain adequate seizure control

- Fetal and maternal risks associated with seizures – tonic clonic seizures carry risks to the mother and fetus and should be avoided where possible.
- Expected course of pregnancy and delivery – these ladies should receive joint care between medical, obstetric and midwifery teams. The birth outcome is usually uneventful and caesarean section is needed only in the most difficult cases.

### Care in Pregnancy

Freedom from seizures is the ultimate goal in the treatment of patients with epilepsy. This is only possible with a multi-professional approach between GPs, midwives, obstetricians and neurologists/Epilepsy Specialist Nurses.

### Antenatal period

Pregnant women with epilepsy should be receiving Joint care from obstetric, medical and midwifery teams

Role of Midwives -

- Booking: The community midwives book these women at home and risk assess them. The woman is booked under the appropriate Consultant depending on the place of delivery - see appendix 1. Should the women require additional discussion regarding her care pathway, she may wish to access a supervisor of midwives.

It is important that along with booking an appointment to the ANC the community midwife also informs the Epilepsy Specialist Nurse /team for an early review.

Opportunity should be taken to give information about importance of continuing to take the medication and to ensure that the woman is taking HIGH DOSE Folic acid (5mg). Information leaflet produced by - Epilepsy Action - ‘Epilepsy and having a baby’ should also be given to the woman.

The community midwife will also review women in between the antenatal clinic visits and liaise with the Obstetrician, Epilepsy Specialist Nurse in case of any problems.

Role of Obstetricians
- The Obstetrician is responsible for the overall care of the woman and will see the women at regular intervals in the antenatal clinic for the Obstetric care and will be responsible for inpatient care if woman needs admission. Each hospital has a lead clinician and the list of current lead is on the appendix(1)

The Obstetrician and ANC midwife will arrange anomaly scan at 18-20 weeks to check for fetal anomalies and further review and scans will be decided as clinical need arises.

The Obstetrician will also liaise with the Neurologist, ESN to put an individualised plan in place.

Role of Epilepsy team- (Neurologist and ESN- Erika Hillman for RGH and Keri John for NHH)
- All pregnant women with Epilepsy should be referred to the Epilepsy clinic, at booking.
- The ESN will aim to see the women as early as possible following intimation of pregnancy by the community midwife and will aim to see women at least once every trimester. The ESN should have an active involvement in the management of Epilepsy and in implementing the plan. She will also take the lead in the registration of these women with the UK Epilepsy and pregnancy register.
- Seizure frequency should be monitored carefully during the pregnancy and adjustments made to AED doses to minimise the number of seizures (particularly generalised tonic clonic seizures).
- The ESN will review these women post natally within general epilepsy clinic.

**Intra-partum period**

Most women with epilepsy will have a normal labour and vaginal delivery- but stress, pain, sleep deprivation, hyperventilation, dehydration increase the risk of seizure in labour(1-4%).

Women should deliver in the obstetric labour ward with one to one care by a midwife, in labour. It is important that both the Obstetric
and Anaesthetic registrars are informed of the admission and the woman has taken her routine medication.

Factors predisposing to increased seizure should be minimised – i.e. ensuring good support to reduce anxiety, adequate hydration and good analgesia.

The usual AED doses should be taken when in labour and continued postnatally. In women unable to tolerate oral medication, AEDs can be given by other routes- consult BNF or pharmacy.

Epilepsy in itself is not an indication for Caesarean section. Caesarean is only performed for Obstetric reasons except if the woman has been having frequent tonic clonic or prolonged complex seizures towards the end of pregnancy.

Analgesia in labour: All of the available methods of labour analgesia can be used with women with Epilepsy safely. There has been concern that high doses of Pethidine may be associated with increased risk of seizures but this is unlikely in the doses used for labour.

**Seizures in labour**

The risk of a seizure during labour for women with epilepsy is 1-2%.

Status epilepticus is characterised by prolonged and persistent seizures and is very rare but is associated with significant increase in maternal as well as fetal mortality and is a medical emergency.

The aim is to terminate seizure as soon as possible using IV lorazepam or diazepam. Please see appendix 2 for guidance on treatment of seizure in hospital.

If there is confusion whether epileptic fit or eclampsia also give slow IV Magnesium Sulphate followed by the infusion for 24 hours. Delivery should be expedited after a seizure in labour eg- ARM, syntocinon augmentation, assisted delivery if in second stage of labour. Caesarean section is usually reserved for Obstetric indications, or if the woman has recurrent seizures or has status Epilepticus.
Postnatal period

Following delivery the drug levels may change again leading to toxicity, particularly if doses have been increased during pregnancy and the dosage needs to be adjusted accordingly. Seizures may be provoked due to fatigue and lack of sleep.

Patient Safety and care of the baby

Pregnant or post-natal women with epilepsy should never be accommodated in a single room (NICE CG137)

All infants born to mothers taking enzyme-inducing AEDs should be given 1mg of vitamin K parenterally at delivery (NICE 2004.) Injuries to infants from maternal seizures (although uncommon), is a possibility, especially if mothers have myoclonic epilepsies. It is important appropriate care is taken when bathing or changing the infant. The leaflet from ‘Epilepsy Action’ Epilepsy and having a baby elaborates on this aspect further.

Extra support should be put in place for mothers with learning difficulties.

Breast feeding

Breast feeding is safe and is to be encouraged. Blood levels of AED in infants are probably lower than in utero provided infant is born healthy and at term 30. If the mother is taking phenobarbitone the infant may become sedated. Neonatal colleagues should be advised of this situation in order to plan the baby’s care.

Contraception

As much as possible the pregnancies should be planned and appropriate contraception is important. Enzyme inducing drugs increase the metabolism and clearance of both estrogens and progesterones, therefore making them less effective leading to more break through bleeding and failures.

<table>
<thead>
<tr>
<th>AEDs which induce hepatic enzymes</th>
<th>AEDs that DO NOT induce hepatic enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine (Tegretol)</td>
<td>Acetazolamide (Diamox)</td>
</tr>
<tr>
<td>Oxcarbazepine (Trileptal)</td>
<td>Benzodiazepines (diazepam, midazolam, lorazepam)</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td></td>
</tr>
<tr>
<td>Phenytoin (Epanutin)</td>
<td>Ethosuximide (Zarontin)</td>
</tr>
</tbody>
</table>
Primidone (Mysolin)  
Topiramate (Topamax)  
Eslicarbazepine (Zebinix)

Gabapentin (Neurontin)  
Lamotrigine (Lamictal)  
Levetiracetam (Keppra)  
Tiagabine (Gabitril)  
Valproate*(Epilim)  
Vigabatrin(Sabril)  
Lacosomide (Vimpat)

In women on enzyme inducing AEDs, higher dose of estrogens and progesterones are necessary, so Oral Contraceptive Pills should contain a minimum of 50mcg and increased to 80 or 100 mcg of Estradiol if necessary. Tricycling the pills in order to reduce number of pill free intervals, is useful. Progesterone only pill or implanon are not recommended. The depot injection is effective but the interval should be shortened to 10 weeks from 12 weeks. Emergency contraception (Levonelle) dose should be increased (doubled) to be effective.

**UK Epilepsy and Pregnancy Register**

All pregnant women with epilepsy, whether or not on medication, should be notified, with their consent, to the UK pregnancy register. This information is useful in assessing the safety of different drugs used to treat epilepsy. Women can self register or a health professional can do this with the woman’s consent by completing a hard copy or website form ([www.epilepsyandpregnancy.co.uk](http://www.epilepsyandpregnancy.co.uk)).

**Staff Education**

Staff Education will be addressed via the day to day clinical training on the maternity unit.

**Written information to women**

The Welsh Risk Pool Standard15: Maternity Services (2011) require women with epilepsy to be given written information during pregnancy relevant to safety measures. Information for women relating to their epilepsy is provided by Epilepsy Action. The ‘Mothers in mind’ booklet includes:
- Understanding epilepsy
- Seizure control
- Epilepsy and the menstrual cycle
- Epilepsy and sexuality
- Epilepsy and contraception
Planning a family
Once you are pregnant
Giving birth
After the birth
Caring for your baby or toddler

Epilepsy Action also provide a ‘Mothers in mind obstetrics resource pack’ and ‘Mothers in mind information resource for health visitors and community practitioners’ available on their website http://www.epilepsy.org.uk/campaigns/awareness/mothersmindprof

NHS Choices provide a web site containing information on epilepsy in pregnancy “The pregnancy care planner” (http://www.nhs.uk). This site can be accessed through the maternity web page on Aneurin Bevan Health Board web site.

Auditable standards

All women should have anomaly scan
All women should see the Epilepsy team at least once in pregnancy
All women should be encouraged to register on the UK Epilepsy register

References

MHRA 2015
Medicines and Healthcare products Regulatory Agency (Jan 2015)

REFERENCES:
2 Welsh Assembly Government (a) (2008), Designed for People with Chronic Conditions, Service Development and Commissioning Directives, Epilepsy: Cardiff


# Appendix-1

## PATHWAY OF CARE FOR PREGNANT WOMEN WITH EPILEPSY IN ABHB

<table>
<thead>
<tr>
<th>Midwifery team</th>
<th>Obstetric Team</th>
<th>Epilepsy team (ESN)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RGH- 4 weekly - Friday am</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NHH- 1st Friday of the month</td>
</tr>
</tbody>
</table>

### 1st Trimester

- **Booking at home**
  - Epilepsy Action leaflet, high dose folic acid, check compliance with treatment. Early booking appointment in joint medical ANC.
  - Referral to Epilepsy team on 01633238528/book into epilepsy CNS clinic.

- **Review and make Obstetric plan**
  - Arrange anomaly scan (letters to specialists, GP.
  - Ensure the midwifery community team are aware of any care plans)

### 2nd trimester

- **Routine screening tests**
  - Anomaly scan
  - Obstetric examination
  - Reiterate advice - medication, personal safety etc

- **Review of results, amendment to care plan**
  - ? need for anaesthetic review

- **Epilepsy frequency and medication review**
  - Reiterate general advice
  - Register pregnancy onto the UK Epilepsy register

### 3rd trimester

- **Routine Obstetric examinations**
  - Discuss labour, labour analgesia, infant care, breastfeeding etc.
  - Arrange parentcraft sessions

- **Consider plan for mode of delivery**
  - Discuss queries about labour book post term IOL etc

- **Epilepsy frequency and medication review**
  - Reiterate general advice and specific to labour, drug levels and dose adjustments in postnatal period etc.
  - Booklet ‘epilepsy and having a baby’
## labour

<table>
<thead>
<tr>
<th>Ensure taken medication</th>
<th>Early review by Obstetric and Anaesthetic registrar</th>
<th>1 to 1 care by midwifery team</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good hydration, analgesia, psychological support</td>
<td>Avoid hyperventilation</td>
<td>Inform on call doctors (Obstetrics, anaesthetics, neonatologists)</td>
</tr>
</tbody>
</table>

## Postnatal period

<table>
<thead>
<tr>
<th>Review of labour events</th>
<th>Review of labour events</th>
<th>Arrange postnatal review (usually at 3/12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encourage breastfeeding</td>
<td>Examination to assess suitability for discharge</td>
<td>ESN review within general epilepsy clinic/Neurologist as appropriate</td>
</tr>
<tr>
<td>Teach infant care and reiterate personal and infant safety. Ensure compliant with medication</td>
<td>Reassurance re: breastfeeding</td>
<td>Drug alteration as necessary</td>
</tr>
<tr>
<td>Strategies to cope with stress and sleep better</td>
<td>Discuss and prescribe contraception</td>
<td>Breastfeeding and contraception</td>
</tr>
<tr>
<td>Give leaflet on ‘After the birth’ and ‘Caring for your infant and toddler’ from Epilepsy action group if patient has not had them. Inform ESN of delivery</td>
<td>Need for good fit control and high dose FA before embarking on next pregnancy</td>
<td>Childcare and Personal safety</td>
</tr>
</tbody>
</table>
Appendix-2
Flow Chart for the management of Epileptic seizure in labour

(NB. In women with no prior history of epilepsy, eclampsia is the most common cause of seizure in labour)

Seizure

- Stay calm, make note of time.
- Ensure woman is safe from injury (move hard objects away)
- Do not restrain the woman or put anything in the mouth
- Allow the seizure to happen (likely to last as long as it usually does - ask family)
- Alert senior midwife, on call Anaesthetic and Obstetric registrar

Once the convulsing stops
- Turn to left side (recovery position) and maintain clear airway (wipe away spit/froth, ensure no block to airway)
- Facial oxygen at 15 L/min
- If have wet themselves deal with this as privately as possible

Yes

Exclude eclampsia:
Check BP / urine for proteinuria
If in doubt commence MgSO4
PET bloods etc
Observe mother

No

Fit short lived (2-3 mins) and spontaneous resolution

Yes

- Give IV Lorazepam up to 4 mg or 10-20 mg rectal Diazepam if no IV access (can be repeated in 10 minutes if necessary)
- If any possibility of eclampsia - give IV Magnesium sulphate 4 grams over 5-10 minutes followed by 1 gram/hour for 24 hours

Observe mother
Check FBC, U&E, LFT, glucose, Coagulation and AED levels

No

Fit stopped

Get senior Medical help
Protect airway,
Commence IV Phenytoin 18 mg/kg slowly (rate not exceeding 50mg per minute)
Continuous ECG, arterial blood gases
 Expedite delivery
Consider transfer to ITU for ventilation