

Womens Guide  
to  
Anti-Convulsant Drugs  
Pregnancy & Effects



Prescribed for Epilepsy, Depression, Pain Relief  
& Migraine Headaches

Anti-Convulsant drugs (AED's) have been prescribed for Epilepsy since 1912, when the first drug, Phenobarbitone was introduced.

There are 3 main medications in the UK known to affect the fetus during pregnancy which are Phenytoin (Epanutin) (1938), Carbamazepine (Tegretol) (1963) and Sodium Valproate (Eplim) (1973).

These three medications have been shown in some cases to cause a constellation of symptoms which go together and are labelled as fetal anticonvulsant syndrome (FACS). Research has demonstrated that the chances of a fetus being affected increases as the medication dose gets higher or where two drugs have been used (polytherapy)

Exposure in the womb to sodium valproate, carbamazepine or phenytoin are linked to an increased risk of developmental difficulties (physical and in terms of learning ability), however not every child may be affected.

Anticonvulsant drugs are typically used to treat seizures; however they are also used to treat certain mental health difficulties, pain and migraine conditions.

FACS can affect a child to varying degrees, ranging from Dysmorphic (unusual) facial features, Cognitive impairments, Spina Bifida, Cleft Lip & Palate etc.... The problems list can be very extensive in some circumstances.

\* Fetal Valproate Syndrome:

This syndrome can occur when the fetus is exposed to

Sodium Valproate (Epilim)

Characteristic Facial features

Developmental Delay (late walking & talking)

Gross & Fine Motor control difficulties

Attention Difficulties

Memory problems

Lower IQ

Speech and Language problems

Visual difficulties

Poor muscle tone ( Hypotonia)

Autistic Spectrum Disorders

Inguinal Hernia

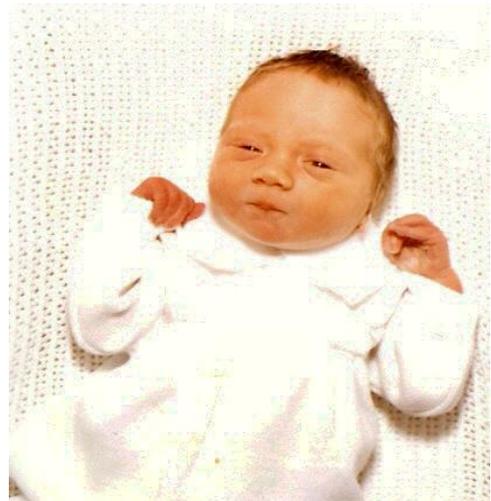
Hypospadias (only in boys)

Limb & Heart Defects

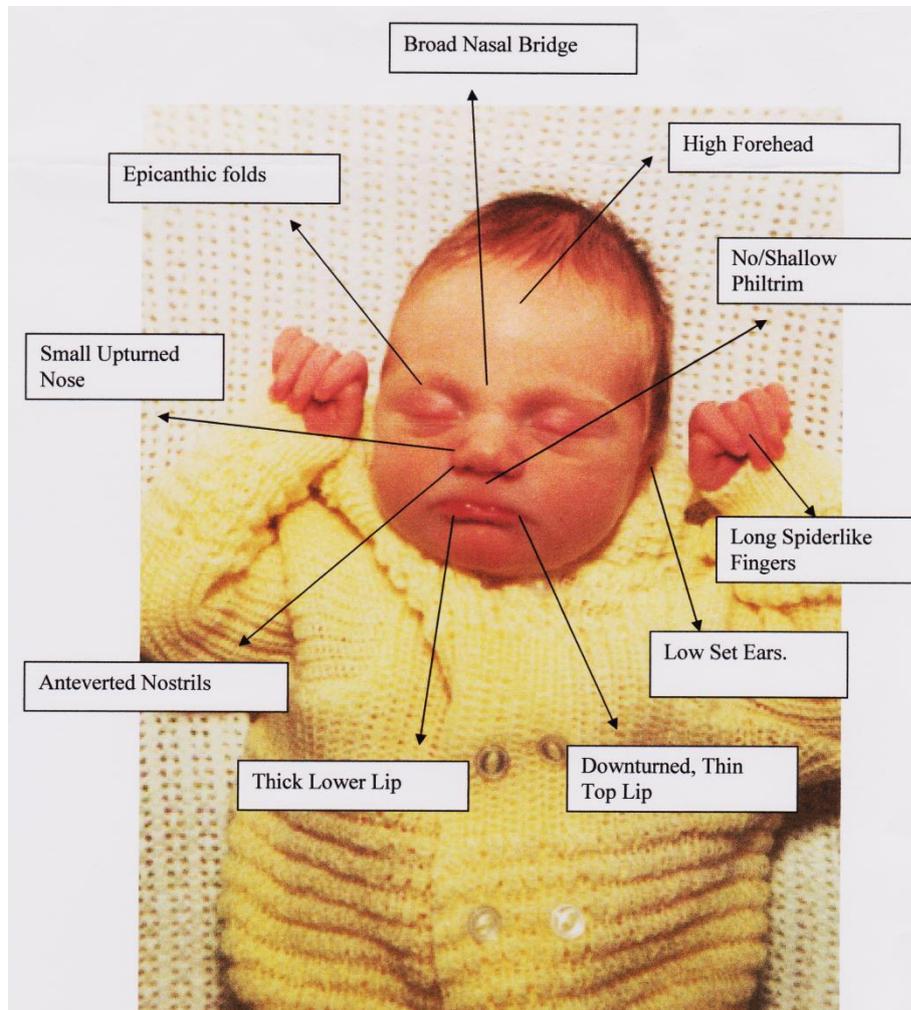
Spina Bifida (failure of the spina column to close properly)

Cognitive difficulties such as: Attention difficulties, Memory problems, Lower IQ and Speech & Language problems.

Difficulties with Social Skills can also occur within people with this condition.



Dysmorphic (unusual) facial features which are associated with Fetal Anti-Convulsant Syndrome are shown below. Not every child will have all the facial features and some may be more prominent than others.



\* Fetal Carbamazepine Syndrome:

Characteristic Facial Features

Nail Abnormalities

Developmental Delay

Lower IQ

Attention & Memory Difficulties

\* Fetal Hydantoin (Phenytoin) Syndrome:

Cleft Lip and/or Palate

Small size at birth

Developmental Delay

Lower IQ

Of course other anti-convulsants may also cause Fetal Anti-Convulsant Syndrome, however the extent of the damages caused by Valproate makes it the worst AED to use during pregnancy for the fetus, and it is important for any woman, with the support of her health care professional to be able to make that informed choice before becoming pregnant.

Fetal Anti-Convulsant Syndrome is an umbrella term for the collective, each medication which affects has its own name for example: if you took Valproate in pregnancy and your child receives a diagnosis this would be Fetal Valproate Syndrome. The symptoms of each drug are extremely similar however we know that babies affected by Carbamazepine for example have more angelic facial features where Valproate's features tend to be of a more a more thick-set look.

We now know that Valproate and other AED's are used for other conditions such as conditions like Bipolar/Depression, Migraine Headaches, and Trigeminal Neuralgia and as a pain relief and so we are aware there may well be more children affected by Fetal Anti-Convulsant Syndrome as first thought.

Please note: Not all children whose mothers have taken an anti-epilepsy drug (AED) during pregnancy may be affected. You must **never** stop taking your medication without medical advice..

## FACS & FIGURES

It is estimated that around 0.5-1% of newborns may be exposed prenatally to an anticonvulsant drug. Sodium valproate reportedly carries the largest risk to developing infants and continues to be prescribed widely across a range of neurological and psychiatric conditions.

Scientific data demonstrates that around 10% of children exposed to sodium valproate will be born with a major congenital malformation (Samran et al 1997), their IQ is likely to be lower (Meador et al 2009), with 29% requiring additional educational support (Adab et al 2001) and with 6% being diagnosed with significant social-communication difficulties such as autism (Bromley et al 2008). With the latest research completed and published on 31<sup>st</sup> January 2013 (Bromley et al 2013) stating ' A 6 or 10 times increased prevalence of neurodevelopmental disorders is reported here for children with a history of prenatal VPA exposure respectively for monotherapy and polytherapy exposure....' 'The increase prevalence of ASD's within this group is consistent with previous retrospective clinical research and reports from animal studies'

Exposure in the womb to anticonvulsant drugs has also been associated with an increased risk to the developing brain causing learning difficulties and Autistic Spectrum Disorders, and the latest research showed that approx. 40% of those affected by Valproate had neurodevelopmental problems/Autistic Spectrum Disorders.

Similar to the findings relating to birth defects the type and dose of an anticonvulsant are important when assessing the level of risk to the developing child. There is less research into this risk but our current level of knowledge suggests that exposure to sodium valproate (Epilim) when the dose is above 1000mg daily carries the largest level of risk. Exposure at this level of sodium valproate (Epilim) has been reported to be associated with increased need for educational support and performance on IQ tests below the majority of their peers.

There is also evidence that children exposed to sodium valproate (Epilim) are at an increased risk of experiencing social-communication difficulties and are at an increased risk of being diagnosed with autistic spectrum disorders.

The evidence for carbamazepine (Tegretol) has been conflicting but, the majority of studies fail to find evidence that children exposed to carbamazepine (Tegretol) experience a higher incidence of learning disability. However, children who have been diagnosed with the physical symptoms associated with prenatal exposure and have a diagnosis of Fetal Carbamazepine Syndrome may be more likely to experience learning difficulties.

As to how many babies are affected each year; through research papers used by INFACT and also the Medicine & Healthcare Products Regulatory Agency (MHRA), and statistics given by the Office of National Statistics (ONS) we know that approximately 20,000 children have been exposed in the UK since Valproate came onto the market in 1973, and that approximately 500 children are affected by Valproate each year, while the figures for Carbamazepine and Phenytonin may have a slightly higher overall figure due to their time on the UK market: Carbamazepine since 1965 & Phenytoin since 1938.

### **New Anti-Convulsants**

It takes a long time to collect data to investigate the longer term health and development of children exposed in the womb and therefore we are currently without adequate information about a number of antiepileptic drugs including:

levetiracetam, topiramate, zonisamide, lamotrigine, gabapentin.

A small amount of research has been conducted which fails to find an association between levetiracetam or lamotrigine and reduced learning ability in children exposed in the womb, although this research mainly comes from a single research group and replication in other cohorts is required before conclusions can be made.

## Pre-Conception Counselling:

Until recently a woman prescribed an AED wishing to become pregnant could be referred for Pre-Conception Counselling, however April 2014 this changed and the section for pre-conception counselling for people with Epilepsy was removed from the Quality and Outcomes Framework (QOF being the annual reward and incentive programme detailing GP practice achievement results).

Your GP is now the person to give you information on AED's in pregnancy albeit not as well detailed as a specialist or counsellor would. It is important to remember that your GP deals with general issues and it may be worth listing the questions you have for him/her, and/or asking for a referral to a Geneticist.

## European Medicines Agency (EMA) Findings:

Until recently the discussion about Anti-Convulsant drugs in pregnancy was left to the discretion of the GP and Neurologist, however on the 10<sup>th</sup> October 2014, following the European Review on Valproate, it was made very clear that Sodium Valproate (Epilim) was not to be prescribed with caution. The report read:

*“Due to the risk valproate poses to unborn children, women who can have children should not take these medicines for epilepsy and bipolar disorder unless other treatments are ineffective or not tolerated”.*

It is understood that there are women who cannot tolerate other medications and so it is extremely important their clinician explains the dangers of Valproate in pregnancy.

For the majority who can tolerate other medications, it is important to avoid Valproate as a first line drug, especially from puberty onwards or if planning to have children in the future.

## Birth & Breastfeeding

We understand the dangers for any pregnant woman during childbirth and the choices and dilemmas she comes across. No doubt most Midwives would opt against Home Birth for a

woman with Epilepsy due to the possibility of seizures and the safest option would be a hospital delivery.

It is necessary to ensure your specialist/Ante Natal Clinic, Midwife and the nurses on the Labour Ward are aware of your Epilepsy and/or the use of any anti-convulsant drug NO MATTER what the condition is you are prescribed it for.

This is so that during and after childbirth your Midwife and the team will be aware and prepared for any complications such as seizures, and also that your baby can be checked over thoroughly for any possible signs of Fetal Anti-Convulsant Syndrome (FACS).

### Folic Acid

We know that many doctors advise and prescribe Folic Acid to women taking anti-convulsant medications for any condition, as it is thought to help avoid any Neural Tube defects, Spina Bifida etc..

However latest research shows that this may not be the case, especially when being prescribed Sodium Valproate. Information was first noted in 2010:

Pharmacoepidemiol Drug Saf. 2010 Aug;19(8):803-7. doi: 10.1002/pds.1975.

### **Does folic acid use decrease the risk for spina bifida after in utero exposure to valproic acid?**

Jentink J<sup>1</sup>, Bakker MK, Nijenhuis CM, Wilffert B, de Jong-van den Berg LT.

*“While folic acid might not be able to reduce the risk for lower spina bifida lesions caused by VPA, the use of folic acid might be important to reduce the risk for higher, folic acid sensitive spina bifida lesions. Further research is needed to get more insight in the most effective form and dose of FA in women that use VPA to reduce the risk for (higher forms of) spina bifida.”*

Journal Neurol Neurosurg Psychiatry 2009; 80: 506-511 doi:10. 1136/jnnp2008 156109

**Folic Acid use and Major Congenital Malformations in Offspring of Women with Epilepsy:  
A Prospective Stud from the UK Epilepsy & Pregnancy Register.**

J I Morrow, S J Hunt, AJ Russell et al..

*“The study supports the view that extrapolation from studies carried out in the general population to groups of women with Epilepsy may be questionable. It may be that the increased risk of MCM recorded in this group occurs through mechanisms other than that of Folic Acid”*

Although more research is needed in this area, we ask women to approach with caution and discuss this at length with their Clinician, Gynecologist, Midwife and/or GP.

### Breastfeeding

Every mother is encouraged by their Midwife to breastfeed their baby as we know this is the best milk for baby during its early days.

However, we are aware that some AED's can be present in the breast milk, and that support groups such as FACSA have noticed an increase in the severity of the child's behavioural difficulties when mum has breast fed her child.

This topic and many more needs to be discussed at any pre-conception counselling appointments, with your Midwife and a Geneticist, if you see one or your Neurologist and GP.

We are aware that the National Institute for Clinical Excellence (NICE) advises Pre-conception counselling for any women taking Anti-Convulsant Drugs to ensure she receives the correct advice concerning the medication she is prescribed, the dose and the affects that her medication may have on the baby during pregnancy.

It is important that any women prescribed an AED receive this advice especially if prescribed Sodium Valproate (Epilim).

## For More Information:

For a more in depth detailed and experienced outlook into Fetal Anti-Convulsant Syndrome and the AED's which may cause problems in pregnancy please contact:

Fetal Anti-Convulsant Syndrome Association:



FACSA was set up to run alongside the Independent Fetal Anti-Convulsant Trust (INFACT). It has a website where women can find the relevant information about AED's in pregnancy, Facebook pages: Fetal Anti-Convulsant Syndrome Association and Epilepsy, Pregnancy & Pills, and also runs a Twitter campaign raising awareness alongside INFACT.

Janet Williams has worked in this field of the voluntary sector of over 20 years, as Founder member of the charity OACS for 13 years and having involvement in a number other projects, while Emma Murphy has had involvement for 6 years being an experienced mother of 5 affected children. Catherine Cox and Saffron Palmer both experienced parents of a FACS child being our latest addition to the board.

### Co-Founders

Emma Murphy  
Janet Williams  
Tel: 01253 799161  
[www.facsa.org.uk](http://www.facsa.org.uk)

### Parental & Educational support

Catherine Cox

### Independent Fetal Anti-Convulsant Trust



Tel: 01253 799161  
[www.facsa.org.uk](http://www.facsa.org.uk)

Company No: 9075755

Janet Williams - Chief Executive Officer

Emma Murphy - Managing Director

Saffron Palmer - Director

Both organisations work together as a team in order to ensure that each parent and their families receive the best support and assistance which can be offered. Taking on all issues of Fetal Anti-Convulsant Syndrome from giving parental advice to Governmental Issues.