



Antiepileptic Drug Pregnancy Registry

SUMMER
2005

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Getting It Right for Women

By Martha Morrell, MD

The health risks associated with particular antiepileptic drugs (AEDs) are an important consideration in treatment selection for our patients, many of whom may require such medication for life. Women with epilepsy are of particular concern due to the impact of both epilepsy and AEDs on fertility, reproductive hormones, pregnancy, fetal outcome and bone health.

Some AEDs, such as carbamazepine, phenytoin, and phenobarbital, reduce the concentration of sex steroid hormones through cytochrome P450 induction, resulting in reduced estradiol concentrations, and increased sex hormone binding globulin¹. Women taking these drugs may therefore experience disorders of sexual desire and sexual arousal.

Valproate increases androgen and insulin levels and is associated with weight gain in 40-50% of patients². Weight gain carries a variety of long term health risks, and so it is important to consider treatments that maintain a normal body weight^{3,4}. Elevated androgen levels and increased sensitivity to insulin may create a polycystic ovary syndrome phenotype^{3,5}. The risk may be highest in women with epilepsy taking valproate at an earlier age^{5,6}. The endocrine and metabolic changes with polycystic ovary syndrome cause significant long-term health consequences. Health care providers should therefore be alert to signs and symptoms and be prepared to intervene should they occur. (continued on page 2)

Publications of the Registry

Wyszynski D.F., Nambisan M., Surve T., Alsdorf R.M., Smith C.R., Holmes L.B. Increased rate of major malformations in offspring exposed to valproate during pregnancy. *Neurology* 2005; 64:961-965.

Holmes L.B., Wyszynski D.F. North American Antiepileptic Drug Pregnancy Registry. *Epilepsia* 2004; 45(11):1465.

Holmes L.B, Wyszynski D.F., Lieberman E.S., The AED (Antiepileptic Drug) Pregnancy Registry: A 6-Year Experience. *Arch Neurol.* 2004; 61:673-678.

Nambisan, M., Wyszynski, D.F., Holmes, L.B. Solutions to some common problems of pregnancy registries: The experience of the AED (Antiepileptic Drug) Pregnancy Registry, *Birth Defects Research* 2003; 67:5.

A North American Registry for Epilepsy and Pregnancy, a unique public/private partnership of health surveillance. *Epilepsia* 1998;39:793-798.

The Registry Staff

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Diego Wyszynski, MD, PhD

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Patients with epilepsy are at increased risk for bone loss and pathological fracture; this risk appears greatest for those with long-term exposure to enzyme inducing AEDs⁷. Selection of an AED that is not associated with bone loss is as important for children, men and reproductive aged women as it is for women in perimenopause and menopause⁸. An increased understanding of the way that some AEDs affect metabolic and reproductive health should help us to get the treatment right the first time, and avoid exposing women to some of the health risks described above.

REFERENCES: ¹ Schipper HM. Sex Hormones and the Nervous System. In Aminoff MJ ed. Neurology and General Medicine. 3rd Edition. Churchill Livingstone; 2001. ² Isojarvi JI *et al.* N Engl J Med 1993;329:1383-1388. ³ Isojarvi JI *et al.* Ann Neurol 1998;43:446-451 ⁴ Biton V *et al.* J Child Neurol 2003;18(2):133-139 ⁵ Mikkonen K *et al.* Neurology 2004;10:445-450 ⁶ Isojarvi JI *et al.* N Engl J Med 1993;329:1383-1388 ⁷ Pack AM *et al.* Epilepsy Behav 2003;4(2):169-74 ⁸ Crabtree N *et al.* Bone 2000;27:151-159

A Message from the Coordinator

My name is Liz Baldwin, and I am the new Coordinator for the AED Pregnancy Registry. Since I've started here, I have received many phone calls and emails from new and old participants. Many of you are searching for the most updated information available on AEDs and pregnancy. We are working very hard to find answers to your questions, but we are only a resource for information. We cannot provide medical advice or counseling; you should always ask your neurologist or psychiatrist for treatment recommendations. However, we also recognize that the experts do not always agree. Please use our website with updated links as a resource. And encourage your health care providers to look at our website and ask questions as well.

For those of you who have enrolled recently, please remember to sign your consent form and send it back to us. Informed consent is an essential element in any research study. We are not able to use the data you provide to us unless we have your signature on our consent form. If you have any questions or concerns regarding the research consent form, or if you need another copy, please call us at 1-888-233-2334 (TOLL FREE). As always, the Registry thanks you for your participation!

Win a \$400 Prize!

Refer a friend or family member to join our control group. You can both win a prize! See page 4 for more information. For complete details please visit www.aedpregnancyregistry.org and click **controls**.

or call (toll free):

1-888-233-2334

Statistics Update

Enrollment:

4328 participants as of June 2005

Participants:

 (data is for the five most commonly used anticonvulsants)

Gravidity:

1st Pregnancy: 37%
2nd Pregnancy: 30%
3rd Pregnancy: 17%
4th + Pregnancy: 16%

Education:

Some high school or less: 21%
Some college: 21%
College: 32%
Post-graduate: 17%

Ethnicity:

White: 86%
Black: 4%
Hispanic: 6%

Health Insurance

Some form of insurance: 97%

Drugs Taken:

23 different monotherapies and 197 different polytherapy combinations

For Your Information!

There are many web sites and online resources available to women with epilepsy and their health care providers. These web sites specifically include information about pregnancy and breastfeeding. The following list is just a small sample of the web sites available to you. Please visit www.aedpregnancyregistry.org for a more comprehensive list of links.

www.otispregnancy.org

Organization of Teratological Information Services primary objective is to educate women and their health care providers about the potential risks of hazardous agents on the developing embryo and fetus.

www.efa.org

The Epilepsy Foundation will ensure that people with seizures are able to participate in all life experiences; and will prevent, control and cure epilepsy through research, education, advocacy and services.

www.seizures.net

Seizures.net publishes recent developments in the treatment of epilepsy. The web site provides information to health care professionals and the public.

www.epilepsy.com

Epilepsy.com exists to inform and empower patients and families living with epilepsy. Epilepsy.com seeks to enable more productive relationships with caregivers, more effective care, and better lives for those with epilepsy.

www.womensmentalhealth.org

MGH Center for Women's Mental Health was designed in an effort to provide scientifically sound and clinically useful information to caregivers and patients at a time when the field of women's mental health is quickly evolving.

Medications being Studied by the AED Pregnancy Registry *:

Ativan® (lorazepam)
Carbatrol® (carbamazepine)
Celontin® (methsuximide)
Depakene® (valproic acid)
Depakote® & Depakote ER (divalproex sodium)
Diamox® (acetazolamide)
Dilantin® (phenytoin)
Felbatol® (felbamate)
Frisium® (clobazam)
Gabitril® (tiagabine)
Keppra® (levetiracetam)
Klonopin® (clonazepam)
Lamictal® (lamotrigine)
Mesantoin® (mephenytoin)
Milontin® (phensuximide)
Mysoline® (primidone)
Neurontin® (gabapentin)
Paradione® (paramethadione)
Peganone® (ethotoin)
phenobarbital (generic)
Phenytek® (extended phenytoin sodium)
Sabril® (vigabatrin)
Serax® (oxazepam)
Tegretol® (carbamazepine)
Topamax® (topiramate)
Tranxene® (clorazepate dipotassium)
Tridione® (trimethadione)
Trileptal® (oxcarbazepine)
Valium® (diazepam)
Xanax® (alprazolam)
Zarontin® (ethosuximide)
Zonegran® (zonisamide)

* This is *not* a complete list. Please call TOLL FREE 1-888-233-2334 to determine if the Registry is studying your specific medication.

AED Pregnancy Registry

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149 CNY- MGH East
Charlestown, MA 02129

PHONE (TOLL-FREE):
(888) 233-2334

FAX:
(617) 724-8307

E-MAIL:
EBaldwin@partners.org

We're on the Web!

Visit us at:

www.aedpregnancyregistry.org

1-888-233-2334
CALL TOLL-FREE



MASSACHUSETTS
GENERAL HOSPITAL



HARVARD
MEDICAL SCHOOL

Congratulations to our Winners!

The AED Pregnancy Registry is pleased to announce the winners of our Spring 2005 Raffle Drawing. The referring participant winner is C. from Texas. With her choice of 5 great prizes, C. selected the Digital Camcorder, valued at \$400. The winner of the control group prize is S. from Minnesota. Also with her choice of 5 great prizes, S. chose the \$400 SuperCertificate from giftcertificates.com.

Congratulations again to our winners! We thank everyone who has referred a friend, or has participated as a member of the control group. We will be conducting another prize drawing in the next few months, so please refer more of your friends and family members to participate in our control group! Please visit our web site at www.aedpregnancyregistry.org for complete details and prize descriptions.

Who Are We Looking For?

The Registry is currently enrolling pregnant women who are taking AEDs for any reason. Participating in the Registry only requires 3 telephone interviews of about 10 minutes each, and all information is kept strictly confidential.

Enrollment is open to women during any stage of pregnancy, but not after the birth of the infant. Ideally, the Registry would prefer to enroll women before they reach the 16th week of pregnancy, or before they have had any prenatal screening. To enroll, or get more information please call the Registry TOLL FREE at **1-888-233-2334**.

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