



# Antiepileptic Drug Pregnancy Registry

WINTER 2008

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## Registry Prepares to Release Monotherapy Data

After collecting, compiling, auditing and analyzing data for 10 years, the Antiepileptic Drug (AED) Pregnancy Registry is pleased to announce that we will soon be releasing our findings on the effect of individual antiepileptic drugs on developing fetuses in the first trimester of pregnancy. Cases where babies are exposed to one drug during pregnancy are known as monotherapy pregnancies and make up the majority of our enrollment. We believe that sharing the results of this monotherapy analysis is a big step towards improving the future care for women who take AEDs while pregnant. This information will help health care professionals and the women they treat make informed decisions concerning the use of antiepileptic medications during pregnancy.

Many people have wondered why the Registry has not released this information until now. Why does it take 10 years? The Registry has taken great care to release its data only once it is proven to be statistically significant. For example, if the Registry had released the data of the first 100 women taking Drug X who enrolled in 1997, the data could have shown 10 malformations, leading us to believe that drug was very unsafe. But, if we kept collecting data from 900 more women taking Drug X, we might find zero malformations in all of those subsequent cases. Malformations in 10 out of 1,000 (1%) is a much different story than 10 out of 100 (10%). Therefore, it is critically important to be sure that data is not showing an increase in risk when it could have been just by chance. *(continued on page 2)*

## A Message from the Registry

Many Registry participants who delivered their babies many months or years ago have recently received forms in the mail to be filled out and returned to us. Why do we need these forms so many years later? We have just completed a detailed audit of the files of all women who have enrolled since the start of the Registry who were taking one AED (monotherapy). In order for each participant's file to be complete we need proof of the woman's consent, a complete initial phone interview, a complete post-partum phone interview, release of a neurology record (or psychiatry record), and the child's pediatric records covering the first six months of life.

If you have recently received these forms in the mail please fill them out so that we can complete your file. *It is never too late to send in your forms.* If you have any questions or concerns regarding the forms you received please do not hesitate to call us TOLL FREE at **1-888-233-2334**. You can also email us at **info@aedpregnancyregistry.org**. We are here to help answer any questions you may have. If you have misplaced your forms, we have them available on our web site at **www.aedpregnancyregistry.org**. As always, the information you give us is strictly confidential and is not accessible to anyone other than Registry staff. Thank you again for your participation!

## The Registry Staff

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## Registry Prepares to Release Data (continued from Page 1)

However, it is also important to understand that there are some drugs for which we only have a very small amount of data. This is due to the fact that there are drugs that are not taken by large numbers of women, and it is possible that we will never have a lot of data for those drugs no matter how long we continue to enroll women.

Our upcoming report will include updated data on drugs that we have published in the past (valproate, carbamazepine, lamotrigine, and phenobarbital), as well as new information about all the other drugs studied by the Registry. We will be publishing data about many of the newer antiepileptic drugs, which have been of great interest to the medical community since the time these medications arrived on the market. The most up-to-date status of our study's publications can be found on our website at [www.aedpregnancyregistry.org](http://www.aedpregnancyregistry.org), under Publications and Press.

While this release of information will be limited to the results of monotherapy pregnancies, we will begin the audit and analysis process for polytherapy data in 2008, with publication to follow in 2009. Polytherapy pregnancies, or pregnancies in which women took more than one anti-epileptic medication in their first trimester, also make up a significant portion of cases in our study. We hope to be able to provide information about the most frequent medication combinations that are seen in these polytherapy pregnancies.

Our ability to publish this important data is due to the continued involvement of our participants. Their dedicated support allows us to keep making steps towards the answers we seek. Without the combined efforts of our participants and the healthcare professionals who treat them, our study would be unable to contribute this kind of knowledge to the field of medicine.

Stay tuned for our upcoming release, and most importantly, please remember that we are still continuing to enroll women and collect data, just as we have been for the past 10 years. The more data we have, the more statistical strength our analysis will have. Please continue to encourage any woman currently taking AEDs for any reason to call us toll free at **1-888-233-2334** to enroll in the Registry.

## Children exposed to valproic acid before birth

The Genetics Unit of Massachusetts General Hospital is looking for children who were exposed to the anticonvulsant drug, valproate, before birth. There has been some concern that prenatal exposure to this drug increases the risk for Autism Spectrum Disorders (ASDs) in some children. We are studying whether the effects of exposure to valproate during pregnancy depend on the child's genetic makeup (the presence of certain genes).

To participate in this study, the children must be at least 2 years of age. The research study would require only a one-day visit as an outpatient free of charge. For some children, the visit would be shorter than an entire day. Participants will receive \$100 for his/her participation, and travel expenses will be reimbursed. If you are interested in participating or would like more information, please contact Uma Deshmukh by calling 617-724-1252 or by e-mail at [udeshmukh@partners.org](mailto:udeshmukh@partners.org). You can also call us at our toll-free number **1-866-354-1523**.

## Statistics Update

**Enrollment:** 6142 participants as of November 2007

### Participants:

#### Gravidity:

1st Pregnancy: 38%  
2nd Pregnancy: 30%  
3rd Pregnancy: 17%  
4th + Pregnancy: 16%

#### Education:

Some high school or less: 21%  
Some college: 25%  
College: 34%  
Post-graduate: 21%

#### Ethnicity:

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

#### Health Insurance

Some form of insurance: 97%

### Drugs Taken:

23 different monotherapies and 197 different polytherapy combinations

## We need your help!

We enroll two different groups of women at the AED Pregnancy Registry. One group is case participants, who are pregnant women taking one or more anti-epileptic drugs. The other group is control participants, pregnant women not taking any AEDs. It is very important for our analyses to have a control group to compare with the women who are taking AEDs in order to better determine the risks of taking AEDs during pregnancy.

We have had many women already call in to participate as controls. Thank you to all the women who have enrolled in our study who have referred their friends and family members. We are so thankful. But we still need your help! If you know of someone who can serve as a control, please ask her to call us TOLL FREE at **1-888-233-2334**.

As a token of our appreciation, each participant who refers a friend or family member that enrolls as control with the Registry will be entered into a drawing to win a \$400 **American Express Gift Card**. In addition, control group members will be entered into a separate drawing to win their own \$400 American Express Gift Card. You both have a chance to win! For every woman you refer as a control, you get one raffle entry. The more women you refer the more chances you have to win the raffle!

## Has your contact information changed?

If your phone number or mailing address has changed or will change before the birth of your baby, please let us know. You can call us toll free at **1-888-233-2334**, or email us at [info@aedpregnancyregistry.org](mailto:info@aedpregnancyregistry.org).

It is important for us to have your updated contact information so that we can contact you to complete your file and keep you informed about the upcoming release of our latest research findings.

## Medications being Studied by the AED Pregnancy Registry \*:

alprazolam (generic)  
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)  
Lyrica® (pregabalin)  
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)  
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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Visit us on the Web:

[www.aedpregnancyregistry.org](http://www.aedpregnancyregistry.org)

**1-888-233-2334**

CALL TOLL-FREE



MASSACHUSETTS  
GENERAL HOSPITAL



HARVARD  
MEDICAL SCHOOL

## The Publications of the Registry

Herndandez-Diaz, S., Smith, C.R., Wyszynski D.F., Holmes L.B. Risk of Major Malformations Among Infants Exposed to Carbamazepine During Pregnancy. *Birth Defects Research (Part A)* 2007; 79:357. (Abstract only)

Holmes L.B, Wyszynski D.F., Baldwin, E.J, Habecker, E., Glassman, L.H., Smith, C.R. Increased Risk For Non-Syndromic Cleft Palate Among Infants Exposed To Lamotrigine During Pregnancy. *Birth Defects Research (Part A)* 2006; 76:5. (Abstract only)

Unger L., Holmes L.B, Wyszynski D.F., Exclusion and Inclusion Criteria For Major Malformations: Impact on Studies of Potential Teratogens. *Birth Defects Research (Part A)* 2006; 76:5. (Abstract only)

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

## Who Can Participate in the Registry?

The Registry is currently enrolling pregnant women who are taking AEDs for any reason. Participating in the Registry only requires 3 telephone interviews. The first interview takes 20 minutes to complete and the next two take 5 minutes each. All information is kept strictly confidential. We are also recruiting controls, please see page 3 for details. 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 16<sup>th</sup> week of pregnancy, or before any prenatal screening. To enroll, or get more information please call the Registry TOLL FREE at **1-888-233-2334**.

**AED Pregnancy Registry**  
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