



ORGANIZATION
OF TERATOLOGY
INFORMATION
SERVICES

For more information regarding OTIS or a Teratology Information Service in your area, call OTIS Information at (866) 626-6847 or visit us online at: www.OTISpregnancy.org.

Tegretol (carbamazepine) and Pregnancy

The information below will help you determine if your prenatal exposure to carbamazepine will increase the fetal risk above the background risk. With every pregnancy, any woman has a 3 to 5 percent chance of having a baby with a birth defect. The information contained in this fact sheet should not be used as a substitute for the medical care and advice of your health care provider.

What is Tegretol?

Tegretol is a medication commonly used to control seizures in the treatment of epilepsy. Tegretol is also used in the treatment of bipolar affective disorder, schizophrenia, trigeminal neuralgia and other specific pain disorders. The generic name of Tegretol is carbamazepine.

I have been taking Tegretol for many years. Can this affect my ability to get pregnant?

Yes. Studies have found that the long-term use of seizure medications in women with seizure disorders is associated with menstrual and infertility problems.

I am taking Tegretol, but I would like to stop taking it before becoming pregnant. How long does Tegretol stay in your body?

The liver breaks down Tegretol; therefore, each individual's ability to break down the medication is different. On average, your body adjusts to Tegretol after 3 - 5 weeks of a treatment with a fixed dose. When a person first starts to take Tegretol, its half-life (the time it takes to eliminate one half of the drug from your body) ranges between 25 - 65 hours. After repeated doses, the half-life decreases to 12 - 17 hours. Therefore, after long-term treatment, most of the Tegretol should be gone from a person's body 3 - 5 days after the last dose.

Please talk to your doctor before you decide to stop taking Tegretol. The benefits of taking the medication for your medical condition, and the possible adverse outcomes of not taking it, may outweigh the benefits of stopping the use of Tegretol in pregnancy.

A pregnant woman also should not change seizure medications (anticonvulsants) during pregnancy without the advice of her doctor. All anticonvulsant medications appear to have some risks for the exposed fetus. Therefore the medication, which best controls seizures for each woman, is the medication of choice for her pregnancy.

Can taking Tegretol during my pregnancy cause birth defects?

Many studies have evaluated Tegretol use for epilepsy during pregnancy. This medication does cross the placenta. In pregnancies exposed to Tegretol during the first trimester, a number of human studies have shown a 1% risk for neural tube defects. The general population risk for having a baby with a neural tube defect, such as spina bifida, is 0.1% (1/1000 births), therefore taking Tegretol in the first trimester of pregnancy will increase the risk for having a baby with a neural tube defect. In addition, some studies have suggested an increase in minor malformations such as a small nose with

a long space between the nose and the upper lip, and small fingernails. Other studies have reported a 2 to 3 times increased risk for major birth defects, such as heart defects and cleft lip, in epileptic women who are taking Tegretol. In addition, some studies have reported an increased frequency of growth retardation and small head size. It is often hard to determine if the birth defects were caused by the medication, the woman's epilepsy, or a combination of both.

Folic acid, a B vitamin, has been found to reduce the risk for neural tube defects and possibly for other structural birth defects in the general population. Because women taking Tegretol have a higher risk of having a baby with a neural tube defect, it is recommended that all women taking Tegretol take 4 mg/day of folic acid before becoming pregnant and during pregnancy. It is not known whether taking folic acid along with Tegretol will reduce the risk for birth defects.

Can taking Tegretol during pregnancy affect my baby's development?

Researchers are just beginning to evaluate the development of children who have been exposed to Tegretol during pregnancy. Some studies have found slightly increased risks for developmental delays in children exposed to Tegretol versus children not exposed to Tegretol or other anticonvulsants. Other studies have found no differences in development in exposed children versus unexposed children. Further research is needed to answer this question completely.

I have been taking Tegretol to control my epilepsy for the last few years and I just found out I am pregnant. What tests are available to see if my baby has spina bifida or other birth defects?

Prenatal testing for neural tube defects (such as spina bifida) is available in pregnancy. There are a few different ways that this can be done. Maternal serum screening (also called the blood test or the triple screen blood test) measures the quantity of a substance called alpha fetoprotein (AFP) in the mother's blood. This protein is made by the fetal liver and crosses into the mother's blood through the placenta. In cases where there is a small hole in the baby's spine or other body structure, the AFP levels are sometimes higher than normal. Having the maternal serum screen around 15 - 20 weeks gestation may help you to know if your baby is at risk. If your AFP level is found to be high, further prenatal testing, such as a specialized ultrasound exam, and/or an amniocentesis, may be offered to you and can help determine if there is an opening in the spine. The maternal serum screen test is usually offered for free by the state in which you live and is normally provided to you by your obstetrician.

Amniocentesis is a test that measures the amount of AFP and the amount of another substance specific to the baby's nervous system, called acetylcholinesterase (ACHE), in the amniotic fluid surrounding the baby. This test is done by taking out a small amount of the amniotic fluid through a needle inserted into the uterus and is usually performed between 17 and 21 weeks gestation. An elevated amount of AFP and presence of ACHE in the amniotic fluid sample can diagnose most open neural tube defects. An ultrasound that looks specifically at the baby's spine can also detect many neural tube defects. Ultrasounds can frequently detect other structural problems and/or birth defects in the baby.

A thorough exam of the baby after birth is also recommended for any woman taking Tegretol during pregnancy. While there is no prenatal test that can detect all birth defects, combinations of these tests will detect a majority of babies that have neural tube defects. All of these options can be discussed with your health care provider.

What could happen to my baby if I stopped taking my Tegretol and then had a seizure during my pregnancy?

Approximately one out of three epileptic women experiences an increase in the frequency of seizures during pregnancy. Complications for mother and fetus can depend on how often she has a seizure and how long they last. Epileptic seizures and convulsions could cause the mother and her fetus to have periods where they do not get enough oxygen in their blood. This could potentially lead to brain damage and developmental issues for the child, or could be life-threatening. In addition, a seizure could cause the mother to fall and physically injure herself and her fetus.

Should I stop taking Tegretol during my pregnancy?

In order to receive the most thorough care during pregnancy, you should contact your health care providers, such as your neurologist and obstetrician, before becoming pregnant to discuss making any changes to your medication or stopping use any time during pregnancy. The benefits of taking Tegretol for your specific situation must be weighed against the potential risks to the developing fetus.

Are there any other concerns with Tegretol use during pregnancy?

In rare instances, maternal use of some seizure medications during pregnancy has been associated with bleeding problems in the newborn due to low vitamin K levels. It is recommended that the woman receive vitamin K supplements in the last month of pregnancy and that the infant receive the routine vitamin K supplement at birth. Women taking Tegretol in pregnancy should consider discussing this with their obstetrician and their child's pediatrician prior to the birth.

Are there any other concerns during pregnancy for women who have epilepsy?

During labor and delivery, a risk of preeclampsia (where the mother's blood pressure rises to the point where it could harm both her and the baby) and premature labor is increased in the woman with epilepsy. It is unknown how severe a seizure must be to be harmful to the fetus.

Can I take Tegretol while breast feeding?

Tegretol is excreted into breast milk. However, the amount of Tegretol found in infant blood is low and does not seem to build up over time. The American Academy of Pediatrics and the World Health Organization considers the drug to be compatible with breast feeding.

April 2003

Copyright by OTIS. Reproduced by permission.

REFERENCES

- Briggs GG et al. (2002) Drugs in Pregnancy and Lactation, a reference guide to fetal and neonatal risk. 6th Ed. Baltimore, MD: Williams & Williams
- Canger R, Battino D, Canevini MP, Fumarola C, Guidonlin L, Vignoli A, Mamoli D, Palmieri C, Molteni F, Granata T, Hassibi P, Zamperini P, Pardi G, Avanzini G. (1999) Malformations in offspring of women with epilepsy: a prospective study. *Epilepsia* 40(9): 1231-36.
- Gladstone DJ, Bologna M, Maguire C, Pastuszak A, Koren G. (1992) Course of pregnancy and fetal outcome following maternal exposure to carbamazepine and phenytoin: a prospective study. *Reprod Toxicol* 6: 257-61.
- Hernandez-Diaz S, Werler M, Walker A, Mitchell A. (2000) Folic Acid Antagonists during pregnancy and the risk of birth defects. *N Engl J Med* 343(22): 1608-1614.
- Jones KL, Lacro RV, Johnson KA, Adams J. (1989) Patterns of malformations in the children of women treated with carbamazepine during pregnancy. *New Engl J Med* 320(25):1661-66.
- Kallen AJB. (1994) Maternal carbamazepine and infant spina bifida. *Reprod Toxicol* 8(3): 203-5.
- Morrell M. (1996) The new antiepileptic drugs and women: Efficacy, reproductive health, pregnancy, and fetal outcome. *Epilepsia* 37(Suppl. 6):S34-S44.
- Nulman I, Scolnik D, Chitayat D, Farkas LD, Koren G. (1997) Findings in children exposed in utero to phenytoin and carbamazepine monotherapy: independent effects of epilepsy and medications. *Am J Med Genet* 68:18-24.
- Ornoy A, Cohen E. (1996) Outcome of children born to epileptic mothers treated with carbamazepine during pregnancy. *Arc Dis Child* 75:517-20.
- Physicians Desk Reference (1999). Montvale, NJ: Medical Economics Data Publishing Company.
- Rosa FW. (1991) Spina bifida in infants of women treated with carbamazepine during pregnancy. *New Engl J Med* 324(10):674-77.
- Samren EB, van Duijn CM, Christiaens GC, Hofman A, Lindhout D. (1999) Antiepileptic drug regimens and major congenital abnormalities in the offspring. *Ann Neuro* 46(5):739-746.
- Scolnik D, Nulman I, Rovet J, Gladstone D, Czuchta D, Gardner A, Gladstone R, Ashby P, Weksberg R, Einarson T, Koren G. (1994) Neurodevelopment of children exposed in utero to phenytoin and carbamazepine monotherapy. *JAMA* 271(10): 767-770.
- Wallace H, Shorvon S, Tallis R. (1998) Age-specific incidence and prevalence rates of treated epilepsy in an unselected population of 2 053 922 and age-specific fertility rates of women with epilepsy. *The Lancet* 352:1970-73.
- Wide K, Winbladh B, Tomson T, Sars-Zimmer K, Berggren E. (2000) Psychomotor development and minor anomalies in children exposed to antiepileptic drugs in utero: a prospective population-based study. *Dev Med Child Neurol* 42:87-92.