



## Seizures & Pregnancy ©2004

It is estimated that 1 in 20 people have an epileptic attack at some time during their life. Seizures may be secondary to a variety of environmental or hereditary disorders. Some types are thought to have a major genetic contribution; however, it is often difficult to predict what the odds would be for a person's offspring to have seizures. Empiric data give a risk of approximately 4% for recurrence of seizures in offspring when one parent is affected, depending on the type of seizure and the causation. There is currently no presymptomatic nor prenatal diagnosis for seizures. It is important for a person to notify his/her offspring's pediatrician of this medical history in order to monitor the infant for any signs of neurological problems.

When a woman with seizures becomes pregnant, there are two things that need to be kept in mind. One is that her seizures need to be controlled during pregnancy in order to avoid major seizures that would decrease the blood supply and therefore, the oxygen supply, getting to the developing baby. Secondly, we would like to use a drug that causes the least risk of problems for the baby to control these seizures.

We usually tell couples that there is a 3% risk for any pregnancy to have a child with a birth defect or health problem regardless of their family medical history. These data come from the pregnancies of mothers who do *not* have any health problems themselves. For the population of pregnant women with seizures, the risk for birth defects is two to three times this risk, particularly for neural tube defects, heart defects and cleft lip/palate.

Anti-seizure medications should not be discontinued in persons when the drug is administered to prevent major seizures. It is extremely harmful for seizures to occur during pregnancy with the major complication being lack of oxygen to the baby, which is life-threatening. Prior to the time of conception and throughout the pregnancy, it is recommended that women discuss the management of their seizure disorder and anti-seizure medication(s) with their neurologist and obstetrician. It is also recommended that women be prescribed 4 mg per day of folic acid to be taken two to three months prior to a future conception and to be continued through the first trimester of a future pregnancy to reduce her risk for neural tube defects to occur.

### **Depakote (Valproic Acid)**

Spina bifida (open spine) is the main malformation associated with the use of Depakote in the first trimester of pregnancy. Anencephaly (open skull) is rarely seen. In the general population, about 1-2 per 1000 babies are born with spina bifida and/or anencephaly. However, the risk of spina bifida among the children of women treated with Depakote during the first trimester of pregnancy is 1-2 percent (or 1-2 per 100 babies). In addition, valproic acid has been associated with a distinctive pattern of anomalies called "the fetal valproate syndrome" which includes postnatal growth retardation, microcephaly, developmental delay, mid-face hypoplasia (underdevelopment), epicanthal folds, short nose, broad nasal bridge, thin upper lip, thick lower lip and micrognathia (small chin).

### **Dilantin (Phenytoin)**

The use of Dilantin during pregnancy has been associated with the "Fetal Hydantoin syndrome", which consists of an unusual and characteristic growth pattern of abnormalities seen in about 10% of infants born to women with seizures who took Dilantin (phenytoin) during pregnancy. Features of this syndrome include a unique facial appearance as well as underdevelopment of fingers, toes, and nails. In addition, some studies show an association between cleft palate, congenital heart disease, microcephaly, developmental delay and prenatal and postnatal growth retardation with the use of

Dilantin during pregnancy. Other authorities believe that the latter anomalies simply occur more often in children whose mothers have seizures in general, regardless of the medications they use to control their seizures during pregnancy.

### **Diazepam (Valium)**

Diazepam is employed as a tranquilizer, muscle relaxant, preoperative medication, and an addition to anticonvulsant therapy. There is a minimal risk to children born after exposure in utero. This information is based on good quantity and quality data. Some neonatal behavior problems have been noted in exposed infants. Initially, there was some evidence of an increased risk for facial clefts (cleft lip with or without cleft palate), but larger studies failed to confirm this finding.

### **Phenobarbital**

The frequency of birth defects appears to be somewhat increased among children of women who take Phenobarbital during pregnancy for treatment of seizure disorders, rather than for other reasons. It is unknown whether this association is due to the seizure disorder itself or to the exposure to phenobarbital. Chronic use of phenobarbital late in pregnancy has been associated with transient neonatal sedation or withdrawal symptoms in infants. Features seen in these infants include hyperactivity, irritability and tremors. Finally, perinatal or neonatal hemorrhage has been observed occasionally in infants of women who took phenobarbital late in pregnancy. This has been attributed to drug induced suppression of synthesis of vitamin K dependent clotting factors.

### **Tegretol (Carbamazepine)**

The use of Tegretol during pregnancy has been associated with an increased risk for spina bifida (a type of neural tube defect) of up to 1% (1/100), as compared to the population risk of 1-2/1000. In addition, Tegretol use during pregnancy has been associated with a unique facial appearance, underdevelopment of the fingers, toes, and nails, and developmental delay in some studies. Some authorities believe that these anomalies may simply occur more often in children whose mothers have seizures in general, regardless of the medications they use to control their seizures during pregnancy.

**Recently, studies have shown that children whose mothers were taking anti-epileptic drugs during pregnancy were more likely to have “additional educational needs.” Valproate and combination anti-epileptic therapy have 2 to 3 fold increase for developmental delay. Tegretol was not associated with an increased risk for developmental delay.**

**Combination of two or more anti-seizure medications may cause a further increase in the risk for birth defects due to the possible synergistic (interactive) effects of the medications.**