Developmental Disabilities, “Autism”, and Birth Defects in Children Exposed Prenatally to Antiepileptic Drugs (AED)

When a woman with epilepsy is pregnant, she and her doctor have to decide whether to continue to use medication to control her seizures. Some of the medications that are used for this disease are known to cause problems for the developing fetus. In addition, these medications are sometimes used to treat other behavior disorders, like bipolar disorder and attention deficit disorder. Among the antiepileptic drugs that cause birth defects are: valproate (valproic acid) (trade name: Depakote), pheytoin (Trade name: Dilantin), phenobarbitone (Phenobarbital), and carbamazepine (Trade name: Tegretol).

The most noticeable birth defect, an increased incidence of spina bifida, is associated with valproic acid. This condition, which involves a failure of the spinal cord to develop properly, is found 10 to 20 times more commonly when valproic acid is used during pregnancy. Facial clefts, heart defects, genital and limb abnormalities are also reported to be associated with this drug. Research has also found that there is a dose-response relationship between the amount of drug used and the severity of response in infants. Other antiepileptic drugs also have an increased incidence of birth defects but the rates seem to be lower than for valproic acid. For all AEDs, the rate is reported to be about 3 times higher than for children whose mothers are not taking these drugs.

Some children also have distinctive physical features that have been called “AED syndrome”. These features include growth retardation, or lower birthweight and birth length. There are also characteristic facial features including a long, thin upper lip, indistinct philtrum
(the groove in the upper lip), epicanthal folds in the eyes, and a mildly flattened appearance to the middle of the face. These features are similar to those seen in fetal alcohol syndrome (FAS).

These drugs also appear to affect the development of the brain leading to problems in development. Among those children who have been studied, the most common developmental problems are delays in development and learning ability and a higher incidence of attention deficit disorder. Valproic Acid was more likely than other AEDs to be associated with these symptoms and the children with physical features were more likely to have developmental problems as well.

Speech delays and “autism” have been reported in children exposed to AEDs. In 2005, researchers estimated that around 10% of children exposed to either valproic acid or other AEDs meet the formal diagnostic criteria for one of the autism spectrum disorders. Other researchers estimate that the rate of autism is 20 times higher in children exposed to AEDs than in the general population.

Currently, it is not yet understood how these drugs produce their negative effects on the fetus while providing mothers with necessary relief from their seizure disorders. A number of explanations have been suggested, including causing a deficiency in folic acid, a nutrient necessary for fetal development. Another suggestion is that AEDs contribute to oxidative stress, which is a naturally occurring process that can affect development when it is excessive or when the body cannot react appropriately.

As a result of the research in this area, physicians usually avoid prescribing AEDs to pregnant women if their medical conditions allow the substitution of other medications. If women are prescribed these drugs, it is usually recommended that they avoid pregnancy or stop
the medications before planning a child. It is often possible to take these steps under medical supervision. This is particularly true when AEDs are being used to treat Bipolar Disorder or Migraine headaches. If women taking these drugs become pregnant, they should consult with their physicians immediately.

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References:


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