

Exposure to valproate during pregnancy can impair a child's cognitive development

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Three-year-olds whose mothers took the antiepileptic drug valproate during pregnancy had average IQs six to nine points lower than children exposed to three other antiepileptic drugs, a landmark multi-center study has found.

The study's authors say that women of childbearing age should avoid valproate as a first choice drug for the treatment of [epilepsy](#). The results are published in the April 16, 2009, issue of the [New England Journal of Medicine](#).

The Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study is following more than 300 children born to women with epilepsy between 1999 and 2004. Investigators at 25 epilepsy centers in the United States and the United Kingdom are participating. At enrollment, the women were taking a single antiepileptic agent: carbamazepine, lamotrigine, phenytoin or valproate.

The NEAD study previously found that valproate exposure also increases the risk of anatomical birth defects, even though it was not designed to look for them.

"There are clear risks associated with valproate, and physicians have an obligation to inform women about them," says lead study author Kimford Meador, MD, professor of neurology at the Emory University School of Medicine. "Valproate still has an important role in treating epilepsy, because some patients' seizures can only be controlled with

valproate. However, we are recommending that women with epilepsy try another drug first."

Around 15 percent of patients with primary generalized epilepsy respond only to valproate, but this selectivity does not apply to other forms of epilepsy, Meador says.

Meador stresses that women who are pregnant and take valproate should not stop without consulting a physician, to avoid seizures with potentially serious consequences.

Valproate's effects on child IQ appear to be dose-dependent, so it may be possible to reduce risk by taking it in lower doses more frequently or in a sustained release formulation, Meador says.

A child's IQ is usually strongly influenced by the mother's IQ. Out of the four antiepileptic drugs studied, only valproate disrupted this relationship.

Preliminary results describing the children's IQs at 2 years of age were reported at the end of 2006. The studies' findings were strengthened by researchers' ability to include more children and measure their progress after three years. The researchers plan to follow the children until age 6.

Valproate is also prescribed for bipolar disorder and migraine headaches. It is sold under the brand name Depakote. Last year the FDA approved a generic version.

More information:

Meador, K.J. et al. Cognitive function at 3 years of age after fetal exposure to antiepileptic drugs N Eng J Med 360: page numbers? (2009).

Meador K.J. et al. In utero antiepileptic drug exposure: fetal death and malformations. *Neurology* 67: 407-412 (2006)

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