

NEWS

Taking meds during pregnancy brings autism risk, benefits

BY EMILY ANTHES

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For a pregnant woman, the factors that can raise autism risk in her unborn child may seem to abound. Studies suggest that **getting the flu, having a fever** or **gaining too much weight** while pregnant can all boost the odds of having a child with autism. Certain medications may also raise the risk. For instance, pregnant women who take the **epilepsy** drug **valproate** are up to seven times more likely to have a child with autism than those who don't.

In the past three months, studies have linked three more types of pills to autism risk: antidepressants, acetaminophen and a class of asthma drugs. Mothers-to-be who take these drugs may as much as double their risk of having a child with autism.

Still, the absolute risk of autism remains small — an important point that **sometimes gets lost** in the alarmist media coverage of these studies. Going off necessary medications can be risky, too. That's why some experts are urging caution in interpreting the results.

"An important issue to keep in mind is that these are indeed large epidemiological studies, and the application of those findings to an individual is going to be more complex," says **Geraldine Dawson**, director of the Duke Center for Autism and Brain Development at Duke University in Durham, North Carolina.

Depression debate:

The link between autism and antidepressants dates back to 2011, when a team of researchers in California reported that prenatal exposure to a class of antidepressants called selective serotonin reuptake inhibitors (SSRIs) **modestly increases the risk of autism**¹.

Two years later, a Swedish study of more than 4,400 people with autism reinforced this finding². But two other large epidemiological studies found no association between antidepressant use

during pregnancy and autism risk^{3, 4}.

A study published late last year in *JAMA Pediatrics* renewed the debate⁵. Researchers led by **Anick Bérard** at the University of Montreal analyzed data from 145,456 children born in Quebec between 1998 and 2009. They used a prescription database to identify pregnant women who filled prescriptions for antidepressants and used medical records and insurance claims to identify children who later received an autism diagnosis.

The researchers found that women who had filled a prescription for antidepressants during the second or third trimester were 87 percent more likely to have a child with autism than those who did not. Women who filled prescriptions for SSRIs, specifically, were more than twice as likely to have a child with autism.

The study received more media attention than any other article published in *JAMA Pediatrics* last year, according to the journal. Bérard is blunt about the findings, saying pregnant women with depression should consider psychotherapy and exercise instead of pills. “Depression needs to be treated, but maybe not with antidepressants for the majority of cases of depression during pregnancy,” she says.

Mood muddle:

But other researchers say the takeaway is not so simple. Bérard and her team identified more than 2,500 children who were exposed to antidepressants during the second or third trimester of pregnancy, and only 31 of them turned out to have autism.

“The vast majority of children who are exposed do not develop autism,” says **Tim Oberlander**, a senior clinician scientist at the Child & Family Research Institute in Vancouver, Canada, who was not involved in the study.

Even if antidepressants raise the risk of autism, they are a minor contributor overall: Of the 1,054 children with autism in the study, 1,008 of them were never exposed to antidepressants.

Less than a month after Bérard’s study, another team reported that maternal depression — not antidepressant use — raises autism risk⁶. The results are in line with **previous findings** showing that women with a history of depression are more likely to have children with autism. The researchers analyzed the electronic health records of 4,650 children, 1,245 of whom have autism, and their mothers.

They found that children with autism are no more likely to have been exposed to antidepressants in the womb than are controls. However, women who took antidepressants before becoming pregnant, or who received psychotherapy during pregnancy, were up to 2.4 times more likely to have a child with autism.

“Really what they're seeing is just a marker of a mom having an illness serious enough that she gets treated with antidepressants,” says lead investigator **Roy Perlis**, associate professor of psychiatry at Harvard Medical School.

Tricky tradeoff:

Women who discontinue antidepressants during pregnancy are more likely to experience a relapse of depression. This carries serious risks of its own: Women with untreated depression are more likely to give birth to small, underdeveloped or premature infants.

A study published 6 January in *Pediatrics* raises similar concerns over common asthma medications. The researchers found that children whose mothers take asthma drugs called **beta-2 adrenergic receptor (B2AR) agonists** either in the 90 days before conception or while pregnant increase their risk of having a child with autism by 30 percent⁷.

But it's difficult to determine whether it is the asthma drugs or the condition itself that drives the risk, says **Craig Newschaffer**, director of the A.J. Drexel Autism Institute at Drexel University in Philadelphia, Pennsylvania.

Uncontrolled asthma during pregnancy can raise the odds of preeclampsia, premature delivery and fetal growth restriction. “I think mothers should be advised to balance this potential hazard against the known benefits of managing your asthma well during pregnancy,” Newschaffer says.

Tough decisions:

Even common over-the-counter drugs may present difficult decisions. A study published 21 December in *Autism Research* raised questions about acetaminophen, a widely used pain reliever — it's the active ingredient in Tylenol — that has long been considered safe during pregnancy⁸.

Researchers followed more than 64,000 children in the **Danish National Birth Cohort**, which enrolled more than 100,000 pregnant women between 1996 and 2002. Women who reported using acetaminophen at any point during pregnancy were approximately 50 percent more likely to have a child with autism and hyperkinetic symptoms, such as hyperactivity and impulsivity. (About one-third of children with autism in the study have such symptoms.)

The study also found a dose-response effect. “The more weeks they have been taking these drugs during pregnancy, the higher the risk,” says lead researcher **Jørn Olsen**, professor of epidemiology at Aarhus University in Denmark.

But the researchers did not find an association between acetaminophen use and autism without hyperkinetic symptoms. And acetaminophen is often used to reduce **fever** which, if left unchecked, can itself **raise a pregnant woman's odds** of having a child with autism.

Overall, the takeaway for pregnant women is that even if some of these drugs do increase the risk of autism, the absolute risk remains extremely low, most experts say.

“Let’s step back, take a breath and look at the evidence,” Oberlander says. “Really, at the end of it, it’s going to be a story about balancing risk and benefit.”

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