

# Study explores possible tie between fever, flu in pregnancy and autism

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Even if higher risk exists, it's still very small, researcher stressed.

(HealthDay)—Children of mothers who contract the flu or have a prolonged fever while pregnant may have a very slight increased risk of developing autism spectrum disorder, a new study suggests.

However, women who have had lasting fever or the flu during pregnancy should not be overly concerned by these results, as the risk seen was extremely small.

Mild infections were not associated with an increased risk of autism, Danish researchers found. Antibiotic use was associated only with a very low, speculative risk, according to the study published online Nov. 12 and in the December print issue of *Pediatrics*.

"[This] study is purely explorative and it is far too soon to suggest any clinical implications," said study lead author Dr. Hjordis Osk Atladottir,

of the Institute of Epidemiology and Social Medicine at University of Aarhus.

"Indeed," she added, "the study shows that around 99 percent of women experiencing influenza, fever or taking antibiotics during pregnancy do *not* have children with autism."

Having an infection triggers the body's immune system, setting off a reaction intended to thwart the danger.

This is good when it comes to defending the body, but studies have suggested that activation of the mother's immune system may harm a fetus's neurodevelopment.

No one knows exactly why this may be the case but, Atladottir said, "previous studies suggest that the activation of the maternal immune system affects the levels of certain cytokines in the maternal blood."

Cytokines are message-carrying cells of the immune system. Some cytokines can cross the placental barrier and, here, may be "able to alter the release of neurotransmitters and thus affect fetal brain development," Atladottir said. She emphasized that this idea is purely speculative.

Another autism expert discussed the possibility that infection in pregnancy could somehow affect an infant's brain development.

Animal studies "suggest that maternal immune infection produces long-lasting changes in the brain, including those seen in individuals on the autism spectrum," said Alycia Halladay, senior director of environmental and clinical sciences at Autism Speaks. "Research suggests specific chemicals, called cytokines, may mediate this effect."

One in 88 children in the United States has an autism spectrum disorder,

according to the U.S. Centers for Disease Control and Prevention. This is an umbrella term for developmental disorders that can range from mild to severe and that often affect social and communication skills. Little is known about what causes autism or precisely why rates seem to be increasing.

For this study, researchers asked mothers of almost 100,000 children born in Denmark between 1997 and 2003 about their history of infection, influenza and antibiotic use during pregnancy.

Children of mothers who reported having the flu while pregnant were twice as likely to develop autism. Having a fever for a week or more was associated with triple the risk.

Common urinary, respiratory and genital infections were not linked with an increased risk, the investigators noted.

Antibiotic use was associated with an almost-dismissible increased risk, although the authors noted that some drugs in this class may affect the function of folic acid, which is essential for fetal neurodevelopment.

But as the authors themselves noted, the study did have a number of limitations, including the fact that the women themselves reported whether or not they had been sick during pregnancy, a potentially unreliable measure.

There's also a possibility that pure chance played a role in the findings, Atladottir said.

"We made over a hundred statistical tests," she said. "The mathematical rule is that around 5 percent of the tests are statistically significant by pure chance. Our few statistically significant findings could thus be the result of coincidence," Atladottir pointed out.

"Thus, we must say that our study is speculative and we have to study this topic further before concluding anything," she said.

U.S. expert Halladay had advice for mothers-to-be.

"Pregnant women should follow the direction of their doctor or health care provider to maintain a healthy pregnancy," Halladay said. "This includes avoiding illness and infection."

While the study found a possible association between maternal infection and autism, it did not prove a cause-and-effect relationship.

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