NEWS

Weak immune response in women may up autism risk in children

BY **ANN GRISWOLD**

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Women who develop infections during pregnancy run an increased **risk of having a child with autism.** Most data indicate that an **overactive maternal immune response** underlies the risk.

But a new analysis runs contrary to this view: It ties high levels of an inflammatory protein in pregnant women to a low risk of autism in their children, suggesting that a strong immune response is protective[1].

Researchers looked at 1,315 mother-child pairs, including 500 children with autism and 235 with developmental delay. They found that healthy pregnant women with high levels of C-reactive protein (CRP), a marker of inflammation, are less likely to have a child with autism than are women with typical levels of the protein. The findings contradict a 2013 report from a large Finnish cohort that tied **high CRP levels during pregnancy** to an increased risk of having a child with autism.

“It was the opposite of what we expected to find,” says senior researcher **Lisa Croen**, director of the Autism Research Program at Kaiser Permanente in Oakland, California. The work appeared in April in *Translational Psychiatry*.

The results suggest that the strength of a woman’s immune system, rather than its response to infection, is the important factor in determining autism risk. Moderate or low baseline levels of CRP might indicate a relatively weak ability to fight off infection. And a less vigorous immune response might boost the risk in some women, the researchers say.

Protective protein:

Immune signals in the womb can push the developing fetus toward autism. Researchers do not know exactly how this process unfolds, but studies implicate various immune molecules, ranging

from antibodies to signaling proteins. In the new study, Croen's team examined levels of CRP, which a person produces at low levels when healthy and at high levels in response to infection, inflammation or trauma.

The scientists measured CRP in frozen blood samples from pregnant women, stored after genetic screening tests. They matched CRP levels with a diagnosis of autism or developmental delay in the children, using California's developmental services database.

The researchers found no association between CRP levels in the women and developmental delay in their children. But women whose CRP levels were in the highest 25 percent of the group had a 44 percent lower chance of having a child with autism than the other women, suggesting that high CRP levels are protective.

In the earlier Finnish study, pregnant women with prenatal CRP levels in the top 10 percent were 80 percent more likely to have a child with autism than those in the bottom 10 percent.

Complex picture:

The opposing results may reflect differences in the study populations. The relatively uniform Finnish population diverges in numerous ways from the Asian, Hispanic, white and black women whose blood Croen and her colleagues examined.

It's possible that genetic differences between the two populations — or exposure to different viruses and bacteria — influence CRP levels, Croen says. Those differences may also affect autism risk. "We really don't know why the results differ," she says. "We're looking at one particular molecule in a sea of thousands of different things that are going on in a woman's body."

These data alone are probably insufficient to untangle the relationship between CRP levels and autism, says **Brian Lee**, associate professor of epidemiology and biostatistics at Drexel University in Philadelphia. "The immune system is dynamic. One measurement over the course of a nine-month pregnancy does not necessarily reflect what's going on across the pregnancy," Lee says.

Croen plans to meet with other researchers later this year to make sense of all the data on maternal immunity and autism risk. Some of the findings fit nicely into a model of immune activation, whereas others, such as those in her new paper, go against the grain.

"It's time to put all the results out on the table and look at the similarities and differences," she says. "It's really the inconsistences that will tell us something."

REFERENCES:

1. Zerbo O. *et al. Transl. Psychiatry* **6**, e783 (2016) **PubMed**