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Elevated maternal C-reactive protein and autism in a national birth cohort.

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Abstract

Autism is a complex neuropsychiatric syndrome with a largely unknown etiology. Inflammation during pregnancy may represent a common pathway by which infections and other insults increase risk for the disorder. Hence, we investigated the association between early gestational C-reactive protein (CRP), an established inflammatory biomarker, prospectively assayed in maternal sera, and childhood autism in a large national birth cohort with an extensive serum biobank. Other strengths of the cohort included nearly complete ascertainment of pregnancies in Finland (N=1.2 million) over the study period and national psychiatric registries consisting of virtually all treated autism cases in the population. Increasing maternal CRP levels, classified as a continuous variable, were significantly associated with autism in offspring. For maternal CRP levels in the highest quintile, compared with the lowest quintile, there was a significant, 43% elevated risk. This finding suggests that maternal inflammation may have a significant role in autism, with possible implications for identifying preventive strategies and pathogenic mechanisms in autism and other neurodevelopmental disorders.Molecular Psychiatry advance online publication, 22 January 2013; doi:10.1038/mp.2012.197.

Vaccine. 2011 Nov 8;29(48):8982-7. doi: 10.1016/j.vaccine.2011.09.039. Epub 2011 Sep 22.

Inflammatory responses to trivalent influenza virus vaccine among pregnant women.

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Abstract

OBJECTIVE:

In the U.S., seasonal trivalent influenza virus vaccine (TIV) is currently universally recommended for all pregnant women. However, data on the maternal inflammatory response to vaccination is lacking and would better delineate the safety and clinical utility of immunization. In addition, for research purposes, vaccination has been used as a mild immune trigger to examine in vivo inflammatory responses in nonpregnant adults. The utility of such a model in pregnancy is unknown. Given the clinical and empirical justifications, the current study examined the magnitude, time course, and variance in inflammatory responses following seasonal influenza virus vaccination among pregnant women.

METHODS:

Women were assessed prior to and at one day (n=15), two days (n=10), or approximately one week (n=21) following TIV. Serum interleukin (IL)-6, tumor necrosis factor (TNF)-α, C-reactive protein (CRP), and macrophage migration inhibitory factor (MIF) were determined by high sensitivity immunoassay.

RESULTS:

Significant increases in CRP were seen at one and two days post-vaccination (ps<05). A similar effect was seen for TNF-α, for which an increase at two days post-vaccination approached statistical significance (p=.06). There was considerable variability in magnitude of response; coefficients of variation for change at two days post-vaccination ranged from 122% to 728%, with the greatest variability in IL-6 responses at this timepoint.

CONCLUSIONS:

Trivalent influenza virus vaccination elicits a measurable inflammatory response among pregnant women. There is sufficient variability in response for testing associations with clinical outcomes. As adverse perinatal health outcomes including preeclampsia and preterm birth have an inflammatory component, a tendency toward greater inflammatory responding to immune triggers may predict risk of adverse outcomes, providing insight into biological mechanisms underlying risk. The inflammatory response elicited by vaccination is substantially milder and more transient than seen in infectious illness, arguing for the clinical value of vaccination. However, further research is needed to confirm that the mild inflammatory response elicited by vaccination is benign in pregnancy.

Brain Behav Immun. 2010 Jan;24(1):49-53. doi: 10.1016/j.bbi.2009.05.055. Epub 2009 May 21.

Depressive symptoms predict exaggerated inflammatory responses to an in vivo immune challenge among pregnant women.

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Abstract

OBJECTIVE:

Stress and depressive symptoms predict exaggerated inflammatory responses to a biological challenge in nonpregnant humans and animals. The extent to which these findings generalize to pregnancy is unknown because the immune system exhibits substantial changes to support pregnancy. Notably, inflammatory responses to infectious agents play a causal role in the development of gestational hypertension as well as risk for preterm birth. Thus, depressive symptoms may increase susceptibility to these outcomes via sensitization of inflammatory processes. The current study was designed to test the hypothesis that depressive symptoms would predict an exaggerated proinflammatory response to an in vivo antigen challenge, influenza virus vaccination, among pregnant women.

METHOD:

Twenty-two pregnant women completed two study visits: baseline and 1week after receiving influenza virus vaccination. Depressive symptoms were measured with the Center for Epidemiologic Studies Depression Scale (CES-D) at baseline. Serum levels of macrophage migration inhibitory factor (MIF) were determined using a high sensitivity immunoassay at both study visits.

OUTCOMES:

Analyses demonstrated that, as compared to those in the lowest tertile of CES-D scores, those in the highest tertile exhibited significantly higher levels of MIF 1week after influenza virus vaccination (p=.035).

CONCLUSIONS:

Depressive symptoms predicted exaggerated MIF production following influenza virus

vaccination during pregnancy. These data support the hypothesis that depressive symptoms are associated with sensitization of the inflammatory response during pregnancy. Thus, women with greater depressive symptoms may be more vulnerable to negative sequelae of infectious illness during pregnancy.

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