In Pregnant Women with COVID-19, Higher Choline Levels May Protect Fetal Brain Development

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Women who develop a COVID-19 infection during the early months of pregnancy have more to worry about than their own health. They must also worry about whether or how their infection will affect the fetus as it develops in the womb.

In such situations, any impact will depend on numerous factors, among which are the timing of the infection and the mother’s nutrition.

COVID-19 is usually not transmitted directly to the fetus. When faced with an infection, the mother's body mounts an immune response. It is this response which poses a potential health risk to the fetus. It is one that changes over time in correspondence with the developmental stages of the fetus.

Newly published research sheds light on how COVID-19, like other respiratory infections, is likely to affect fetal brain development and what can be done to minimize harmful impacts. The focus is on a crucial developmental window occurring around the beginning of the second trimester of pregnancy.

This is the moment when the emerging brain begins to build neural circuitry that can inhibit excitatory signals in neural networks. When robust neural inhibition fails to emerge prior to birth, past research has demonstrated that after birth, the child will be at significantly increased risk for behavioral problems and for developing illnesses including autism, attention-deficit disorder and schizophrenia.

Preventing such outcomes has been a high priority in research at the University of Colorado School of Medicine led by BBRF Scientific Council member Robert Freedman, M.D. Dr. Freedman, a two-time BBRF Distinguished Investigator and 2015 winner of the BBRF Lieber Prize, has demonstrated how levels of the essential nutrient choline in the mother’s serum (the portion of the blood that does not include clotting factors) correlate with the fetus’ ability to develop proper neural inhibition.

Since many pregnant women have diets that are deficient in choline, Dr. Freedman and colleagues have strongly recommended dietary...
supplementation with choline or phosphatidylcholine, sometimes called lecithin.

That advice is renewed in the context of COVID-19 infection during pregnancy, in a new paper appearing in the Journal of Psychiatric Research, authored by Dr. Freedman with colleagues including M. Camille Hoffman, M.D., 2015 BBRF Baer Prize winner; Amanda Law, Ph.D., BBRF Scientific Council member, 2011 Baer Prize winner, and 2006 Young Investigator; and Sharon Hunter, M.D., a 2003 BBRF Young Investigator.

The team drew upon data collected in their prior studies of women who developed infections (bacterial and viral) during the first 16 weeks of pregnancy—the point at which the fetus is most vulnerable to maternal inflammation. They assumed, per guidance from the U.S. Centers for Disease control (CDC), that COVID-19 infection would affect fetal development in ways similar to other respiratory coronaviruses have in the past.

The team compared 36 pregnant women who had developed moderate to severe respiratory infections by week 16 with 53 mothers who reported no inflections. Choline levels were determined at week 16 in both groups, and at other time points. When infants reached 3 months of age, their mothers completed an extensive questionnaire seeking to gauge the infants' duration of attention, their ability to enjoy quiet play, their cuddliness and engagement with parents and caretakers, and their soothability. (The researchers call these “regulatory” measures.)

The team made two major findings, both suggesting the importance of women getting adequate amounts of choline during pregnancy.

The first finding was about children of mothers who had respiratory infections during the first 16 weeks of pregnancy. At 16 weeks, when mothers had choline levels at or above the minimum level advised by the FDA—the equivalent of 550 mg per day—their children 3 months after birth were better able to pay attention and to form a bond, compared with children of mothers whose choline levels were below the FDA daily minimum at 16 weeks.
The second finding was that children of infected mothers with adequate choline levels fared just as well when compared with children of mothers who had no infection during pregnancy.

“Higher choline levels obtained through diet or supplements,” the team concluded, “may protect fetal development and support early behavioral development even if the mother contracts a viral infection in early gestation when the brain is first being formed.” Importantly, choline levels are most important early in pregnancy—levels beginning at 22 weeks were not observed to affect infant outcomes.

Although the FDA’s current suggested minimum dietary requirement for choline is 550 mg, Dr. Freedman and colleagues continue to advocate for higher levels, noting that supplements containing 900 mg of choline “have been safely used during pregnancy from 15 weeks gestation until delivery, with subsequent positive effects on the child’s attention and social behavior through 3 and a half years of age.”

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