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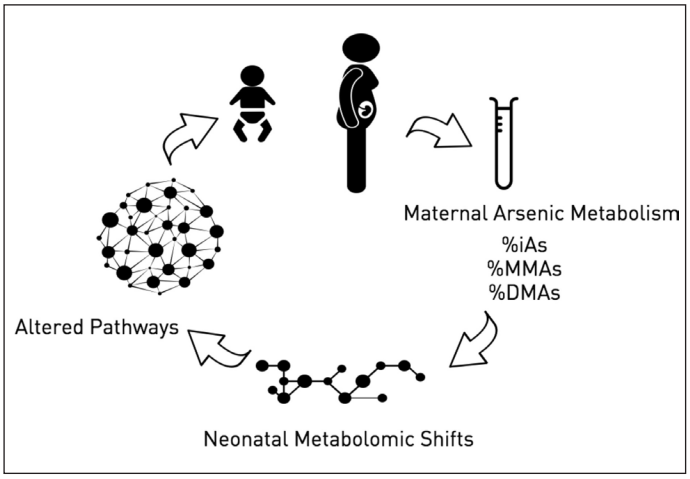
Prenatal Arsenic Exposure Alters Newborn Metabolite Profiles

Researchers at the University of North Carolina at Chapel Hill Superfund Research Program (UNC SRP) Center have identified metabolites in umbilical cord blood that are associated with exposure to arsenic in the womb. The findings also show that differences in a mother's metabolism of arsenic may influence the metabolite profile of her baby. Assessing changes in the newborn's metabolite profile by looking at the full range of metabolites, or metabolome, may provide insight into how prenatal arsenic exposure could affect important pathways responsible for maintaining normal cell processes in the body.

Linking Arsenic Exposure to Metabolome Shifts

In the new study, researchers led by Rebecca Fry, Ph.D., including first author Jessica Laine, examined associations between prenatal arsenic exposure and the neonatal metabolome. The mothers and children they studied were part of the Biomarkers of Exposure to Arsenic (BEAR) pregnancy cohort in Gomez Palacio, Mexico, where women have been exposed to a wide range of arsenic levels in their drinking water.[1]

They used a metabolomic approach coupled with systems toxicology-based analytical techniques to assess hundreds of metabolites in cord blood. They conducted a metabolomics analysis to determine whether arsenic and its breakdown products, monomethylated arsenicals (MMAs) and dimethylated arsenicals (DMAs), in maternal urine and cord blood were associated with these cord blood metabolite patterns. The researchers identified 10 metabolites with altered levels in cord blood that were associated with arsenic and its breakdown products in maternal urine. They also identified 17 metabolites that were associated with arsenic in cord blood. Among these metabolites, 11 were previously identified by the research group as common across a separate arsenic-exposed population, including creatinine, glutamine, methionine, and succinate.[2]



This research provides evidence that changes in the neonatal metabolome may be linked to prenatal arsenic exposure, with implications for later life health effects. Reprinted with permission from Laine et al. 2017. Neonatal metabolomic profiles related to prenatal arsenic exposure. Environ Sci Technol 51:625-633. Copyright 2017 American Chemical Society.

They also examined the proportion of MMAs to DMAs in urine because previous studies have associated a higher proportion of MMAs to DMAs with less efficient arsenic metabolism and negative health outcomes, including lower birthweight as well as adult urinary bladder cancer and skin cancer. They found an association between an increased proportion of DMAs in maternal urine and decreased methionine, which plays an important role in the body's arsenic metabolism. Because a higher percentage of DMAs is indicative of potential increased metabolism efficiency, these findings suggest that differences in arsenic metabolism of the mother during pregnancy may also be associated with metabolic differences in the child.

Identifying Potential Pathways to Disease

The metabolites identified in the study are linked to important biological pathways in the body and could provide insight into mechanisms through which prenatal arsenic exposure may cause disease. For example, succinate is involved in the citric acid (TCA) cycle, which is responsible for generating energy in the body. Previous studies have suggested that arsenic metabolism may impede the TCA cycle, resulting in insufficient energy production. Other altered metabolites

identified by the researchers play a role in how our body metabolizes vitamins and amino acids, which may affect our body's defenses, among other processes.

According to the researchers, metabolomics may be a useful method to determine biological markers of diseases associated with arsenic and also may provide insight into mechanisms that influence disease development.

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[1] Laine JE, Bailey KA, Rubio-Andrade M, Olshan AF, Smeester L, Drobna Z, Herring AH, Styblo M, García-Vargas GG, Fry RC. 2015. Maternal arsenic exposure, arsenic methylation efficiency, and birth outcomes in the Biomarkers of Exposure to ARsenic (BEAR) pregnancy cohort in Mexico. Environ Health Perspect 123:186-192.

[2] Martin E, Gonzalez-Horta C, Rager J, Bailey KA, Sanchez-Ramirez B, Ballinas-Casarrubias L, Ishida MC, Gutierrez-Torres DS, Hernández Ceron R, Viniegra Morales D, Baeza Terrazas FA, Saunders RJ, Drobna Z, Mendez MA, Buse JB, Loomis D, Jia W, Garcia-Vargas GG, Del Razo LM, Styblo M, Fry R. 2015. Metabolomic characteristics of arsenic-associated diabetes in a prospective cohort in Chihuahua, Mexico. Toxicol Sci 144:338-346.

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To learn more about this research, please refer to the following source:

Laine JE, Bailey KA, Olshan AF, Smeester L, Drobna Z, Styblo M, Douillet C, Garcia-Vargas G, Rubio-Andrade M, Pathmasiri W, McRitchie S, Sumner SJ, Fry RC. 2017. Neonatal metabolomic profiles related to prenatal arsenic exposure. Environ Sci Technol 51:625-633. doi: 10.1021/acs.est.6b04374 PMID: 27997141