Treatments for asthma and pre-term labor may increase risk of autism in developing fetus

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Commonly prescribed beta 2 adrenergic agonist drugs for the treatment of asthma in pregnant women as well as pre-term labor may increase the incidence of autism-spectrum disorders, psychiatric pathology, cognitive problems and poor school performance in their children, according to a new study published in the December 2009 issue of the *American Journal of Obstetrics & Gynecology*.

Beta 2 adrenergic agonist drugs as a class are widely used in obstetrics as tocolytics to inhibit or slow down labor and bronchodilators, but may act as functional and behavioral teratogens when given continuously in the mid to late second or early third trimesters. By correlating the basic science and clinical data, investigators observed that when given prenatally, these drugs can cause functional and behavioral disorders by permanently altering the balance of sympathetic and parasympathetic tone in the individual. Animal studies support the concept that in humans prenatal exposure to continuous high doses of beta 2 adrenergic agonists can permanently dysregulate signaling from the beta 2 adrenergic receptor.

Researchers show how sympathetic overactivity and disease are correlated, citing studies that show the association between in utero exposure to beta 2 adrenergic agonists in humans and later development of these conditions.

The authors also offer recommendations for safe practice in obstetrics in light of the teratogenic risk posed by beta 2 adrenergic agonists.

Writing in the article, Frank R. Witter, MD, , Johns Hopkins University School of Medicine and Johns Hopkins University Bloomberg School of Public Health, and co-authors state, "Given the risk of long-term neurophysiologic and behavioral impairment, the use of beta 2 adrenergic agonists should be limited to proven indications when alternate drugs are ineffective or unavailable and the risks of the untreated disease to the mother and fetus are greater than the risk of the beta 2 adrenergic agonist. Treatment duration should be as short as clinically feasible. Further ongoing surveillance of the use of these agents in pregnancy is needed to refine the parameters for their safe use in pregnancy. Future pharmacogenetics research is also needed to better characterize the highest risk group for teratogenesis from these agents."

Echoing the concerns, Roberto Romero, MD, Chief, Perinatology Research Branch, Program Director for Obstetrics and Perinatology, Intramural Division, NICHD, NIH, DHHS and Associate Editor of the *American Journal of Obstetrics & Gynecology*, states that "The observations reviewed by the authors call for a re-examination of the commonly accepted safety of these agents during pregnancy."

More information: The article is "In Utero Beta 2 Adrenergic Agonist Exposure and Adverse Neurophysiologic and Behavioral Outcomes" by Frank R. Witter, MD, Andrew W. Zimmerman, MD, James P. Reichmann, MBA, and Susan L. Connors, MD. It appears in *American Journal of Obstetrics & Gynecology*, Volume 201, Issue 6 (December 2009) published by Elsevier.

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