The Complex Etiology of Autism Presents Challenges in Risk Communication

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Research has revealed a complicated genetic architecture and a variety of environmental factors that increase risk for autism spectrum disorder (ASD).\textsuperscript{1} In fact, the more we learn about potential risk factors associated with ASD, the more complex the search for causal mechanisms becomes. Epidemiologic studies, like that by Gidaya et al\textsuperscript{2} published in this issue of Pediatrics, provide important information on modifiable exposures that increase the risk of ASD. The study by Gidaya et al found that exposure during pregnancy to a class of drugs used for treating asthma or allergies, β-2 adrenergic receptor (B2AR) agonists, is associated with a modest increase in risk for ASD. Asthma or allergies during the second trimester is also associated with higher risk for ASD. Gidaya et al’s study, however, included maternal asthma as a covariate, and the association between exposure to B2AR agonists during pregnancy and increased ASD risk remained. Given that uncontrolled maternal asthma can potentially negatively influence fetal development, the risk versus benefit of using B2AR agonist drugs during pregnancy must be carefully weighed.

As research sheds light on the etiology of ASD, there is a parallel need to focus on how best to communicate these findings to patients and the general public.\textsuperscript{3} Translating research findings into guidance for the public is complicated and must be highly individualized. Studies such as this one by Gidaya et al provide important starting points to examine characteristics in the population and specific exposures. However, questions remain about the mechanisms that result in the association. Studies with rodents demonstrated that B2AR agonist drugs given to pregnant rats altered neuronal development and synaptic proteins involved in neurotransmission. Much more work is needed to know if a similar mechanism is occurring in some humans and how this may result in the development of ASD.

The finding of an association between B2AR agonist drugs and ASD adds to a growing number of environmental exposures during the prenatal period that can influence fetal brain development and are associated with modest increases in risk for ASD. These include diseases during pregnancy such as gestational diabetes mellitus, drugs such as valproic acid and thalidomide, dietary factors such as folic acid deficiency, and exposure to high levels of pesticides and air pollution.\textsuperscript{4} Other factors associated with ASD include advanced parental age,\textsuperscript{5} extreme premature birth,\textsuperscript{6} and short interpregnancy interval.\textsuperscript{7} Each child with ASD represents a unique combination of both genetic and environmental risk factors. Individually, each of these risk factors is not sufficiently common in the population, nor does it confer a high enough risk for ASD, to result in a sizeable impact on ASD prevalence.\textsuperscript{8} Finding common pathways across
these factors and how they work within specific biologic contexts will ultimately be essential to understanding the paths leading to ASD.9

Service providers play an important role in disseminating and translating findings regarding risk factors for ASD. Findings are sometimes relatively straightforward and actionable, such as a recommendation to take prenatal vitamins and minimize exposure to toxins such as pesticides. In other instances, the findings and decision-making are nuanced and complex, such as a decision whether to take B2AR agonist drugs during pregnancy when uncontrolled asthma also has a negative influence on fetal development. There is a need for service providers, researchers, and the media to provide the public with accurate, timely, and relevant information about the growing body of evidence related to genetic and environmental risk factors for ASD, and at the same time, take care that such information is comprehensible, balanced, and meaningful, leading to informed decision-making and optimal outcomes for children.

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