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Genetic Syndromes, Maternal Diseases and Antenatal Factors Associated with Autism Spectrum Disorders (ASD)

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Autism spectrum disorder (ASD) affecting about 1% of all children is associated, in addition to complex genetic factors, with a variety of prenatal, perinatal, and postnatal etiologies. In addition, ASD is often an important clinical presentation of some well-known genetic syndromes in human. We discuss these syndromes as well as the role of the more important prenatal factors affecting the fetus throughout pregnancy which may also be associated with ASD. Among the genetic disorders we find Fragile X, Rett syndrome, tuberous sclerosis, Timothy syndrome, Phelan–McDermid syndrome, Hamartoma tumor syndrome, Prader-Willi and Angelman syndromes, and a few others. Among the maternal diseases in pregnancy associated with ASD are diabetes mellitus (PGDM and/or GDM), some maternal autoimmune diseases like antiphospholipid syndrome (APLS) with anti-β2GP1 IgG antibodies and thyroid disease with anti-thyroid peroxidase (TPO) antibodies, preeclampsia and some other autoimmune diseases with IgG antibodies that might affect fetal brain development. Other related factors are maternal infections (rubella and CMV with fetal brain injuries, and possibly Influenza with fever), prolonged fever and maternal inflammation, especially with changes in a variety of inflammatory cytokines and antibodies that cross the placenta and affect the fetal brain. Among the drugs are valproic acid, thalidomide, misoprostol, and possibly SSRIs. β2-adrenergic receptor agonists and paracetamol have also lately been associated with increased rate of ASD but the data is too preliminary and inconclusive. Associations were also described with ethanol, cocaine, and possibly heavy metals, heavy smoking, and folic acid deficiency. Recent studies show that heavy exposure to pesticides and air pollution, especially particulate matter <2.5 and $10\,\mu m$ in diameter (PM2.5 and PM10) during pregnancy is also associated with ASD. Finally, we have to remember that many of the associations mentioned in this review are only partially proven, and not all are "clean" of different confounding factors. The associations described in this review emphasize again how little we know about the etiology and pathogenesis of ASD. It is obvious that we need more epidemiologic data to establish many of these associations, but if proven, they might be promising avenues for prevention.

Keywords: ASD, genetic syndromes, autoimmune diseases, prenatal factors, inflammation, drugs, chemicals, pollution

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