Autistic spectrum disorders (ASD) are common neurobehavioral syndromes characterized by deficits in social interactions, impaired communication skills and repetitive stereotypic behaviors expressed by 3 years of age (1). Recent studies of these disorders indicate a strong genetic component but specific aetiologies and pathogeneses are usually unknown (1–3). Concordance for ASD is 90% in identical twins compared to 10% for dizygotic twins and siblings.

In recent years the incidence of ASD has increased throughout the world (4). Although changes in diagnosis might be a likely explanation, synergistic, environmental factors may account for part of the increased incidence of this serious disorder (5,6).

In some cases, a disorder that includes autistic features is an identifiable syndrome due to a chromosomal abnormality (e.g. Fragile X), a single gene mutation (e.g. Rett's Syndrome), an intrauterine infection (e.g. Rubella) or a metabolic disease (1). Mitochondrial cytopathies are among the metabolic disorders that continue to be associated with ASD in case reports (7–15). In larger series of people with autism but no diagnosis of a mitochondrial cytopathy, biochemical markers of mitochondrial dysfunction were found with variable frequency (14–17). These metabolic abnormalities may be elevated blood levels of lactate and pyruvate indicative of impaired aerobic glycolysis. In one study of 69 children, 20% had elevated blood lactates with five showing abnormalities at sites in the mitochondrial electron transport chain (17). In another study of 210 people, 17% had elevated blood lactates and 28% had elevated lactate/pyruvate ratios (15). The role of abnormal energy metabolism in the pathogenesis of autism might be related to the brain’s dependence on aerobic glycolysis (18).

My colleagues and I recently have found support for the view that mitochondrial dysfunction contributes to the clinical phenotype of ASD. Lymphoblasts from autistic people who donated blood to the Autism Genetic Resource Exchange (AGRE) had maximal respiratory rates that were 40–50% higher than lymphoblasts from near same-gender relatives who were not diagnosed as autistic (p < 0.01) (19). This difference was present in all 9 cell pairs studied. In 7 of 9 cell pairs, we observed inhibition of electron transport in the first segment (Complex I) of the electron transport chain. These findings suggest that the increased cellular respiratory capacity in lymphoblasts from autistic donors is an adaption to partial inhibition of ATP synthesis. We do not think that mitochondrial disorders account for all instances of autism in children who do not have a recognizable syndrome. Rather, we feel that disorders of ATP synthesis or its regulation, due to a mitochondrial cytopathy, may be present in a larger-than-expected part of the autistic population, regardless of the family history of ASD or clinical metabolic disease.

The increasing awareness that mitochondrial cytopathies may contribute to the pathogenesis of ASD in an appreciable percentage of people with this diagnosis has very limited implications for the current treatment or management of autism. Clearly, effective treatments for the mitochondrial cytopathies are not yet available, even though numerous nutritional supplements and vitamin supplements are frequently used. Should the paediatrician want to or be requested to screen for a mitochondrial cytopathy, blood tests (e.g. lactic acid and pyruvic acid) are appropriate. More expensive or invasive radiologic or tissue studies are not advised unless additional information suggests they are indicated for a specific child. Appropriate evaluations of other organ functions (e.g. gastrointestinal, cardiac, kidney, vision or hearing) should be considered as indicated.

While environmental factors may affect the clinical state of patients with diseases of energy metabolism, there is no evidence that any such effects cause ASD. In the United States, the Vaccine Compensation Board decided that vaccines ‘significantly aggravated an underlying mitochondrial disorder’ causing brain damage with ‘features of autism spectrum disorder’ (20). As a paediatric neurologist with an interest in the causes and treatments of both autism and...
mitochondrial encephalopathies, I know of no evidence in the scientific literature to support the conclusion that vaccinations damage the brains of children with mitochondrial diseases. It is of the greatest importance that we continue to vaccinate children to minimize/eliminate the possibility of brain damage due to diseases including measles, mumps and rubella.

I encourage paediatricians to respond to requests from autism researchers for access to their autistic patients. The search for mutation sites and for environmental factors that might influence the occurrence of ASD needs many subjects. Most important, a role of energy metabolism in the pathogenesis of ASD suggests new directions to search for the prevention and amelioration of this disabling disorder.

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References