

A Case-Control Study of Mercury Burden in Children with Autistic Spectrum Disorders

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ABSTRACT

Large autism epidemics have recently been reported in the United States and the United Kingdom. Emerging epidemiologic evidence and biologic plausibility suggest an association between autistic spectrum disorders and mercury exposure.

This study compares mercury excretion after a three-day treatment with an oral chelating agent, meso-2,3-dimercaptosuccinic acid (DMSA), in children with autistic spectrum disorders and a matched control population. Overall, urinary mercury concentrations were significantly higher in 221 children with autistic spectrum disorders than in 18 normal controls (Relative Increase (RI)=3.15; $P < 0.0002$). Additionally, vaccinated cases showed a significantly higher urinary mercury concentration than did vaccinated controls (RI=5.94; $P < 0.005$). Similar urinary mercury concentrations were observed among matched vaccinated and unvaccinated controls, and no association was found between urinary cadmium or lead concentrations and autistic spectrum disorders.

The observed urinary concentrations of mercury could plausibly have resulted from thimerosal in childhood vaccines, although other environmental sources and thimerosal in Rh₀(D) immune globulin administered to mothers may be contributory.

Regardless of the mechanism by which children with autistic spectrum disorders have high urinary mercury concentrations, the DMSA treatment described in this study might be useful to diagnose their present burden of mercury.

KEY WORDS: autism, autistic spectrum disorders, chelation, DMSA, mercury, thimerosal

Background

Recent studies have analyzed the prevalence of autism from the mid-1980s through 2002 in the United States and the United Kingdom.¹⁻⁵ The prevalence of autism is estimated to have risen from one in about 2,500 children in the mid-1980s to as common as one in 150 by 2002. Further, since all of these studies find the prevalence of autism in males to be four times that of females, the male prevalence of this disorder exceeds one in 100. These studies show that the rise in the prevalence in autism is genuine and not the result of population migration, differences in diagnostic criteria, or other potential confounders.

In 2001, the Institute of Medicine (IOM) of the United States National Academy of Sciences⁶ determined that a link between mercury from thimerosal contained in childhood vaccines and the recent dramatic increase in neurodevelopment disorders is biologically plausible. Recent studies demonstrate a strong epidemiologic

link between exposure to mercury from thimerosal contained in childhood vaccines and neurodevelopment disorders.⁷⁻⁹

The purpose of this study was to evaluate the concentration of mercury in the urine following a three-day treatment with an oral chelating agent, meso-2,3-dimercaptosuccinic acid (DMSA), in children with autistic spectrum disorders in comparison to a control population. Forman et al.¹⁰ have reported on the use of oral treatment with DMSA in children exposed to metallic mercury. The authors found that oral chelation with DMSA produced a significant mercury diuresis in these children. They observed no adverse side effects of treatment. The authors concluded that DMSA appears to be an effective and safe chelating agent for treatment of pediatric overexposure to metallic mercury. In addition, extensive literature supports its safety in the chelation of lead from exposed children.

Methods

This study is a retrospective analysis of 221 consecutive children with previously established autism spectrum disorders referred and admitted to the International Child Development Resource Center (ICDRC). Each child had been diagnosed with autism (DSM-IV 299.00) or pervasive developmental disorder (DSM-IV 299.80) by outside physicians. A control population of 18 children was also identified without autism spectrum disorders in themselves or among their siblings or their first-degree family members. These healthy children presented to the ICDRC for elective determination of their levels of environmental mercury exposure at the request of their families, and are included here for case comparison. The Arizona State University Institutional Review Board approved our retrospective examination of cases and controls in this study.

All children were examined to exclude those who had dental amalgams. Among the 221 cases, all had received their full scheduled childhood immunizations appropriate for their respective ages. Among the 18 controls, 10 children had received their full childhood immunization schedules, and 8 children had received no childhood immunizations because of religious objections.

Informed consent was obtained from both cases and controls for DMSA chelation treatment. Controls and cases were both challenged with a three-day oral treatment of DMSA (10 mg/kg per dose given three times daily). After the ninth dose, the first voided morning urine was collected (when possible), or an overnight urine collection bag was worn. All laboratory analyses were performed by the Doctors' Data, Inc., in Chicago, Ill. The response to DMSA was measured as micrograms of mercury per gram of creatinine using inductively coupled mass spectrometry, and creatinine was measured using the Jaffe method. The laboratory was not informed whether the specimens were from cases or controls.

In addition to the overall excretion data, several epidemiologic case-control studies were conducted using the available populations. First, it was possible to match 88 cases against 16 controls for age (within one year) and sex, and overall post-DMSA urinary