

## A prospective study of thimerosal-containing Rho(D)-immune globulin administration as a risk factor for autistic disorders

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### Abstract

**Background.** This study evaluated the relationship between prenatal mercury exposure from thimerosal (49.55% mercury by weight)-containing Rho(D)-immune globulins (TCRs) and autism spectrum disorders (ASDs).

**Methods.** The Institutional Review Board of the Institute for Chronic Illnesses approved the present study. A total of 53 consecutive non-Jewish Caucasian patients with ASDs (*Diagnostic and statistical manual of mental disorders, fourth ed.* – DSM IV) born between 1987 and 2001 who presented to the Genetic Centers of America for outpatient genetic/developmental evaluations were prospectively collected from June 1, 2005 through March 31, 2006. Imaging and laboratory testing were conducted on each patient to rule out other causal factors for their ASDs. As race-matched controls, the frequency of Rh negativity was determined from 926 non-Jewish Caucasian pregnant women who had presented for outpatient prenatal genetics care to the Genetic Centers of America between 1980 and 1989.

**Results.** Children with ASDs (28.30%) were significantly more likely (odds ratio 2.35, 95% confidence interval 1.17–4.52,  $p < 0.01$ ) to have Rh-negative mothers than controls (14.36%). Each ASD patient's mother was determined to have been administered a TCR during her pregnancy.

**Conclusion.** The results provide insights into the potential role prenatal mercury exposure may play in some children with ASDs.

**Keywords:** *Developmental delay, ethylmercury, rhogam, thimerosal, thiomersal*

### Introduction

Autism spectrum disorders (ASDs) are neurodevelopmental disorders characterized by impairments in social relatedness and communication, repetitive behaviors, abnormal movement patterns, and sensory dysfunction [1,2]. While genetic factors are recognized as being important in the pathogenesis of ASDs, a role for environmental factors has received considerable attention. For example, Beversdorf et al. reported that pathological changes in the cerebellum in autism are thought to correspond to an event before 30–32 weeks of gestation [3]. These researchers determined that a higher incidence of prenatal stressors was found in autism at 21–32 weeks of gestation, with a peak at 25–28 weeks, and concluded that their data supported the possibility of prenatal stressors as a potential contributor to autism. Additionally, researchers reported that exposure to mercury can cause immune, sensory, neurological, motor, and behavioral dysfunctions

similar to traits defining or associated with autistic disorders, and that these similarities extend to neuroanatomy, neurotransmitters, and biochemistry [4–7].

Rho(D)-immune globulin is an immune globulin preparation containing antibodies to Rho(D) that is intended for intramuscular injection. Prior to late 2002/early 2003 when the last doses of thimerosal-containing Rho(D)-immune globulin preparations expired, most formulations of Rho(D)-immune globulin contained thimerosal. Thimerosal is an ethylmercury-containing compound (49.55% mercury by weight) that was added to Rho(D)-immune globulin preparations at the preservative level of 0.003–0.01%. Rho(D)-immune globulin is used to prevent isoimmunization in the Rho(D)-negative individual exposed to Rho(D) positive blood as a result of fetomaternal hemorrhage occurring during delivery of an Rho(D) positive infant, abortion (either spontaneous or induced), or following amniocentesis or abdominal trauma. Rh hemolytic