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A Prospective Study of Mercury Toxicity Biomarkers in Autistic Spectrum Disorders

David A. Geier
Institute of Chronic Illnesses, Silver Spring, Maryland, USA

Mark R. Geier
Genetic Centers of America, Silver Spring, Maryland, USA

Porphyrins are derivatives formed in the heme synthesis pathway and porphyrins afford a measure of xenobiotic exposure. The steps in the heme pathway most vulnerable to heavy metal inhibition are uroporphyrin decarboxylase (UROD) and coproporphyrinogen oxidase (CPOX) reactions. Mercury toxicity was associated with elevations in urinary coproporphyrin (cP), pentacarboxyporphyrin (5cxP), and precoproporphyrin (prcP) (also known as keto-isocoproporphyrin) levels. Two cohorts of autistic patients in the United States and France had urine porphyrin levels associated with mercury toxicity. A prospective study of urinary porphyrin testing at LabCorp (United States) and the Laboratoire Philippe Auguste (France) involving 71 autism spectrum disorder (ASD) patients, neurotypical sibling controls, and general population controls was undertaken. ASD patients had significant elevations in urinary levels of cP, 5cxP, and prcP relative to controls, and > 50% of ASD patients had urinary cP levels more than 2 standard deviations above the mean values for neurotypical sibling controls. Significant reductions in urinary 5cxP and cP levels were observed in ASD patients following chelation. A significant correlation was found between urinary porphyrins measured at LabCorp and those measured at the Laboratoire Philippe Auguste on individual ASD patients. The established developmental neurotoxicity attributed to mercury and biochemical/genomic evidence for mercury susceptibility/toxicity in ASDs indicates a causal role for mercury. Urinary porphyrin testing is clinically available, relatively inexpensive, and noninvasive. Porphyrins need to be routinely measured in ASDs to establish if mercury toxicity is a causative factor and to evaluate the effectiveness of chelation therapy.

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David Geier has been a consultant in cases involving vaccines/biologics before the no-fault National Vaccine Injury Compensation Program and in civil litigation. Dr. Mark Geier has been an expert witness and consultant in cases involving vaccines/biologics before the no-fault National Vaccine Injury Compensation Program and in civil litigation. David and Mark Geier have a patent pending for the treatment of autistic disorders.

Address correspondence to Mark R. Geier, MD, PhD, President, The Genetic Centers of America, 14 Redgate Ct., Silver Spring, MD 20905, USA. E-mail: mgeier@comcast.net

Porphyrins are derivatives of the heme synthesis pathway that afford a measure of xenobiotic exposure (Brewster, 1988). Heme production primarily occurs in liver, kidneys, and erythroid cells. The synthetic process is summarized in Figure 1 (Nataf et al., 2006). Excess porphyrinogen metabolites are excreted in the urine as oxidized porphyrins, particularly uroporphyrin (uP) and coproporphyrin (cP), the most abundant soluble porphyrin molecules in the kidney cortex (Woods & Miller, 1993). Because these mid-pathway porphyrins are the most water-soluble of all the porphyrins, they are excreted predominantly in urine, whereas the hydrophobic protoporphyrin is predominantly found in the bile and feces.

Excess urinary porphyrin excretion, or porphyrinuria, results from inhibition of key enzymatic steps in conditions including genetic deficiencies in heme production enzymes (Sarkany, 1999), hepatitis, renal disease, and erythroid disease (Gross et al., 2000), as well as by heavy metal inhibition of heme enzyme synthesis (Woods, 1996). Both in experimental animals and in humans exposed to heavy metals, elevated levels of porphyrins are found in the urine (Bowers et al., 1992; Woods, 1996). The steps in the heme pathway most vulnerable to heavy metal inhibition are those in which uroporphyrin decarboxylase (UROD) (Woods & Kardish, 1983) and coproporphyrinogen oxidase (CPOX) (Woods et al., 2005) are involved. The result of these inhibitions is specific elevations of cP and pentacarboxyporphyrin (5cxP) in the urine. A causal relationship between heavy metal inhibition and porphyrinuria was demonstrated both in rats (Pingree et al., 2001) and humans exposed to mercury (Woods et al., 1993), as well as in humans exposed to lead (Rosen & Markowitz, 1993). Investigators also observed that heavy metal removal with chelating agents reduced urinary porphyrin levels to control values (Gonzalez-Ramirez et al., 1995). Although nonmetal agents