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IMPORTANT INSIGHTS REGARDING NEW TESTING AND TREATMENT FOR AUTISM SPECTRUM DISORDERS

BY DAVID A. GEIER, BA, MARK R. GEIER, MD, PHD, FABMG, FACE, AND LISA K. SYKES, MDIV

Autism spectrum disorders are neurodevelopmental disorders that affect at least 1 child in 150 in the United States. They disproportionately affect male children (five boys diagnosed for every one girl). Currently, a diagnosis of an ASD is based upon observations made by a physician of early onset of impairments in social interaction, communication, and unusual stereotyped behaviors. The child diagnosed with an ASD generally shows little interest in the world or people around him, and most exhibit a wide range of profound behavioral problems and delayed or undeveloped skills. Furthermore, a child diagnosed with an ASD may display a range of problem behaviors, such as hyperactivity, poor attention, impulsivity, aggression, self-injury, and tantrums. In addition, many often display unusual responses to sensory stimuli such as hypersensitivities to light, certain sounds, colors, smells, or touch, as well as having a high threshold of pain.¹

In contrast to the previous notion that a diagnosis of an ASD is exclusively based upon an observational profile for a child, newly emerging research suggests that many of these children have demonstrable medical abnormalities. Identifying the medical abnormalities associated with an ASD diagnosis is now possible through the use of routine clinical laboratory testing. In the patient with an ASD, clinical tests should be run to assess urinary porphyrins,

transsulfuration metabolites, mitochondrial dysfunction, and hormones.

Urinary Porphyrins

Researchers have identified a well-established specific biomarker for environmental exposure, which recently has been utilized in the treatment of patients diagnosed with an ASD. Porphyrins, derivatives of the heme (as found in hemoglobin) synthesis pathway, provide a means to measure environmental exposures.² Recent studies conducted on three separate continents have examined urinary porphyrins in patients diagnosed with an ASD, and in each of these studies, mercury-associated urinary porphyrins were significantly elevated in comparison to controls.³⁻⁸ These observations are consistent with other recent data demonstrating increased brain mercury levels,⁹ increased blood mercury levels,¹⁰ increased mercury levels in baby teeth,¹¹ increased mercury levels in hair samples,¹² increased mercury in urine/fecal samples,^{13,14} and decreased excretion of mercury through first baby haircuts^{15,16} among individuals diagnosed with an ASD relative to controls. In addition, mercury-associated urinary porphyrins were increasingly elevated across the autism spectrum. The higher the level of mercury-associated urinary porphyrins, the more severe the ASD diagnosis (Asperger's disorder < pervasive developmental delay – not otherwise specified < autism < autism +

epilepsy). Furthermore, using the Childhood Autism Rating Scale (CARS), a recognized test of ASD severity, researchers found a significant and increasing correlation between mercury-associated urinary porphyrins and CARS scores prior to blinded lab testing.⁴ In order to help lower urinary porphyrins, chelation therapy, a medical treatment that helps to remove heavy metals from the body, resulted in significant reductions in mercury-associated urinary porphyrins in patients diagnosed with an ASD.⁶⁻⁸

Porphyrins can be examined in patients diagnosed with an ASD using Laboratory Corporation of America (LabCorp) random fractionated urinary porphyrin testing. Additionally, 2,3-dimercapto-1-propanesulfonic acid (DMPS) and *meso* 2,3-dimercaptosuccinic acid (DMSA), previously shown to significantly lower mercury body burden (and hence lower urinary porphyrins) and to help reduce mercury-associated neurodevelopmental toxicity,¹⁷ may improve clinical outcomes for patients diagnosed with an ASD.^{18,19}

The Autism Research Institute reported survey data collected from over 22,300 parents of children with ASD diagnoses.¹⁹ The survey includes a list of 45 medications,²³ non-drug supplements or biomedical treatments, and nine special diets used to treat ASD diagnosed patients. The parents rated the treatments on a six-point scale. Parents, assessing their children's condition before and after treatment, rated chelation therapy (or the removal of heavy metals) as the highest or best of these 77 choices. Seventy-six percent of parents said that their child "got better" on this treatment.

Transsulfuration Metabolites

Glutathione, sulfate, and cysteine are key substances in the transsulfuration pathway that help the body to excrete mercury, and recent studies on patients diagnosed with an ASD have revealed significant abnormalities in the level of these metabolites. When compared to controls, patients diagnosed with an ASD have a decreased level of these metabolites that coincides with a decreased ability of patients to excrete mercury. These differences among individuals help to explain why children with similar mercury exposure patterns may have different clinical outcomes.²⁰



The transsulfuration pathway may be evaluated by LabCorp; this includes homocysteine, cystathionine, glutathione, and taurine testing. Supplementation with targeted nutritional interventions using cofactors to help the transsulfuration pathway, such as methylcobalamin (vitamin B-12), folic acid, and pyroxidine (vitamin B-6), in ASD diagnosed patients with transsulfuration abnormalities help to improve clinical and laboratory findings.²¹⁻²³

Mitochondrial Dysfunction

Recent research has supported a role for mild mitochondrial dysfunction among patients diagnosed with an ASD. Investigators reported that values of free and total carnitine and pyruvate were significantly reduced, while ammonia and alanine levels were considerably elevated, in patients with an ASD diagnosis. These are suggestive of mild mitochondrial dysfunction.²⁴ Furthermore, investigators have reported clinical symptoms of mild mitochondrial dysfunction in patients diagnosed with an ASD including low muscle tone, motor coordination problems (gross and fine), and fatigue or low energy.²⁵ Mercury exposure at low doses is known to cause mitochondrial damage consistent with that observed in patients diagnosed with an ASD.²⁶

Mitochondrial dysfunction tests available from LabCorp include carnitine, pyruvic acid, lactic acid, and ammonia. Treatment of the

mitochondrial dysfunction present in many patients diagnosed with an ASD may include administration of CARNITOR® (L-carnitine).²⁷ With sufficient CARNITOR® dosing, patients diagnosed with an ASD may experience improvements in low muscle tone, motor coordination problems, and fatigue or low energy.

Hormones

The ratio of ASD cases between the sexes, with five boys diagnosed to every one girl, likely reflects a male vulnerability to developing an ASD, a hypothesis supported by multiple lines of evidence. This male vulnerability likely indicates an important role for mercury exposure as a causal factor in ASDs. In animal models and in human poisonings, males were found to be significantly more susceptible to mercury toxicity than females. Also, in a series of tissue culture experiments, testosterone (the male hormone) was able to increase the neuronal toxicity of mercury, whereas estrogen (the female hormone) decreased the toxicity. Further, increased testosterone was observed to occur in tissue culture, in animals, and in humans following low-dose mercury exposure. Finally, mercury exposure was found to significantly increase testosterone synthesis by inhibiting the conversion of a key regulator metabolite called dehydroepiandrosterone (DHEA) to the storage metabolite called dehydroepiandrosterone-sulfate (DHEA-S).²⁸⁻³² As a result, the body's regulation of testosterone production is disabled, and this causes excessive levels of testosterone.

Individuals diagnosed with an ASD were found to have evidence of significantly increased pre- and postnatal levels of testosterone and significantly decreased pre- and postnatal levels of estrogens. Individuals diagnosed with an ASD also tend to display traits associated with high levels of testosterone and low levels of estrogens, including hypermasculine profiles on many cognitive tasks, changes in play patterns, decreased eye contact, decreased socialization, lower verbal and higher numerical intelligence, and brain hemispheric asymmetries. Consistent with this phenomenon, studies of patients with naturally higher testosterone levels were found to display significantly higher numbers



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of autistic traits than controls.^{29,33-35}

Clinical examinations of patients diagnosed with an ASD reveal that girls with an ASD diagnosis (and even other family members) show a significant delay in the onset of menarche (excess androgens have been linked to menstrual problems) and are more likely to display elevated rates of testosterone-related medical disorders than neurotypical controls. Among the conditions found to be significantly increased in patients diagnosed with an ASD and/or in their families are hirsutism (excessive hair growth); bisexuality or asexuality; irregular menstrual cycle; dysmonorrhea; polycystic ovary syndrome; severe acne; epilepsy; tomboyism; and family/personal history of ovarian, uterine, breast, and prostate cancers, tumors or growths. In addition, boys diagnosed with an ASD revealed elevated rates of diagnosed premature puberty.³³⁻³⁵ Finally, a cohort study of 70 consecutive patients with an ASD diagnosis revealed that their blood samples, collected and analyzed at LabCorp, showed significantly increased average levels of serum testosterone, serum free testosterone, percent free testosterone, DHEA, and androstenedione in comparison to controls.²⁹

Testosterone and estrogen testing available from LabCorp includes testicular

function profile II, dehydroepiandrosterone, dehydroepiandrosterone-sulfate, androstenedione, androstane diol glucuronide, dihydrotestosterone, estradiol, estrone, and total estrogens.

A clinical trial study of the use of anti-testosterone medications in a cohort of patients diagnosed with an ASD was previously reported. The anti-testosterone therapeutic agent of LUPRON® (leuprolide acetate) supplemented with oral ANDROCUR® (cyproterone acetate) were found to significantly lower testosterone levels while simultaneously helping to significantly reduce autistic-like behaviors. In some of the patients examined, significant autistic behavior improvements occurred within days of administration of LUPRON®, such as better sleep patterns, improvements in attention and hyperactivity, and increased socialization. In addition, LUPRON® therapy helped to significantly ameliorate clinical symptoms/behaviors associated with elevated testosterone in the blood, such as early growth spurt, early secondary sexual changes (e.g., masturbation), body and facial hair, and aggressive behaviors that may be observed among some children diagnosed with an ASD. Finally, anti-testosterone therapy helped to quantitatively and significantly lower ASD symptoms measured

using the Autism Treatment Evaluation Checklist (ATEC) in the areas of socialization, sensory/cognitive awareness, and health/physical/behaviors skills¹⁸ within about three months of therapy.

In subsequent clinical use of LUPRON® administration to nearly 200 patients diagnosed with an ASD (from young children to young adults), this therapy was found to produce significant ameliorations in hyperactivity/impulsivity, stereotypy, aggression, self-injury, abnormal sexual behaviors, and/or irritability behaviors that frequently occur in patients diagnosed with an ASD, with few non-responders to the therapy. Furthermore, LUPRON® helped to lower blood testosterone levels significantly and was found to have minimal adverse clinical effects.²⁹ Other drugs with known anti-testosterone effects, such as ALDACTONE® (spironolactone), may also have beneficial effects on patients diagnosed with an ASD.³⁶ Menstrual-aged females with an ASD diagnosis may benefit additionally from increased estrogen levels from YAZ® (drospirenone/ethinyl estradiol).²⁷

Conclusion

Clearly, after examination of the aforementioned biomarkers, an ASD diagnosis encompasses more than simply observations by a physician. ASDs have a biological basis as demonstrated in clinically available lab testing, and currently utilized observational symptoms used in the diagnosis of an ASD neglect the importance of medical evaluations and testing. The emerging biomarkers delineate a common denominator of mercury intoxication as an important causal factor for many patients diagnosed with an ASD.

As the biomedical understanding of autism advances at a quickening pace, new testing and treatments are becoming increasingly available. Blood and urine testing is essential in understanding ASD medical symptoms and working with individual cases. Even more information may now become available helping to make differential diagnoses, perhaps with causal contributing factors. This is an encouraging time with important possibilities for all who live and work with ASDs.

Information on testing and treatment clinics across the US can be found on the web at www.asdcenters.com.

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