

## ORIGINAL RESEARCH

## Maternal Chemical and Drug Intolerances: Potential Risk Factors for Autism and Attention Deficit Hyperactivity Disorder (ADHD)

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**Purpose:** The aim of this study was to assess whether chemically intolerant women are at greater risk for having a child with autism spectrum disorders (ASD) or attention deficit hyperactivity disorder (ADHD).

**Methods:** We conducted a case-control study of chemical intolerance among mothers of children with ASD (n = 282) or ADHD (n = 258) and children without these disorders (n = 154). Mothers participated in an online survey consisting of a validated chemical intolerance screening instrument, the Quick Environmental Exposure and Sensitivity Inventory (QEESI). Cases and controls were characterized by parental report of a professional diagnosis. We used a one-way, unbalanced analysis of variance to compare means across the 3 groups.

**Results:** Both mothers of children with ASD or ADHD had significantly higher mean chemical intolerance scores than did mothers of controls, and they were more likely to report adverse reactions to drugs. Chemically intolerant mothers were 3 times more likely (odds ratio, 3.01; 95% confidence interval, 1.50–6.02) to report having a child with autism or 2.3 times more likely (odds ratio, 2.3; 95% confidence interval, 1.12–5.04) to report a child with ADHD. Relative to controls, these mothers report their children are more prone to allergies ( $P < .02$ ), have strong food preferences or cravings ( $P < .003$ ), and have greater sensitivity to noxious odors ( $P < .04$ ).

**Conclusion:** These findings suggest a potential association between maternal chemical intolerance and a diagnosis of ADHD or ASD in their offspring. (J Am Board Fam Med 2015;28:461–470.)

**Keywords:** Attention Deficit Hyperactivity Disorder, Autism Spectrum Disorder, Chemical Exposure, Chemical Intolerance, Maternal Exposure

Developmental disorders, including autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD), now affect 1 in 6 children in the United States,<sup>1</sup> a trend that is changing the spectrum of patients who visit family physicians.

According to the Centers for Disease Control and Prevention, ASDs now affect 2% of US children,<sup>2</sup> an 8-fold increase since the early 1990s.<sup>3</sup> ADHD affects 9.5% of children ages 4 to 17 years, up 5.5% per year for the period between 2003 to 2007.<sup>4</sup> Proposed reasons for the recent increase in ASD cases include greater awareness, changes in diagnostic criteria, and younger ages at diagnosis. However, these factors seem to account for only one third of the increase in ASD since the early 1990s.<sup>3</sup>

How are these prevalence changes affecting primary care practice? First, compared with children with asthma, children with ADHD are 3.5 times

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more likely to have an unmet medical need.<sup>5</sup> Children with ASD often suffer from comorbid asthma, allergies, recurrent ear infections, immune system dysfunction, and gastrointestinal disorders, further increasing the demand on primary care practices.<sup>6,7</sup> Primary care physicians are often first to recognize ASD or ADHD and are uniquely positioned to coordinate care for these families,<sup>8</sup> but they feel less able to treat children with ASD compared with typically developing children, citing a lack of knowledge of available resources and insufficient training.<sup>9</sup>

### **Environmental Exposures Can Adversely Affect Neurodevelopment**

Gene–environment interactions underlie both ASD and ADHD. Recent twin studies estimate that genes account for about 38% of the heritability of autism, whereas environmental factors account for 58%.<sup>10</sup> Children are especially vulnerable to adverse effects from toxic exposures. Numerous studies of humans demonstrate an association between chemical exposures and impaired neurodevelopment.<sup>11–13</sup> Prenatal exposure to organophosphorus pesticides is a risk factor for the development of ASD<sup>14</sup> and ADHD,<sup>15</sup> and is known to impair neurodevelopment in children.<sup>16</sup> Proximity to vehicle traffic and coal-fired power plants also are recognized risk factors for both ADHD and ASD.<sup>17–19</sup> Since World War II, the types and levels of volatile organic chemicals inside homes and offices, where people in developed countries spend 90% of their day, have increased dramatically.<sup>20</sup> Among the chemical exposures implicated in ASD are styrene, vinyl flooring, methylene chloride, elemental mercury, and antibacterial quinolone.<sup>21,22</sup>

A number of medications used during pregnancy increase the risk of ASD and ADHD.<sup>23,24</sup> Strong evidence supports a causal relationship between ASD and in utero exposure to the medications valproic acid, thalidomide, and misoprostol.<sup>25–29</sup> For example, thalidomide taken early in pregnancy is associated with autism and, if taken later, may result in the characteristic limb deformities (phocomelia).

### **Chemical Intolerance**

Chemical intolerance (CI) affects an estimated 10% to 30% of the US population and occurs worldwide across a range of demographic groups and ages.<sup>30–35</sup> These individuals typically report adverse effects from low-level exposure to a wide variety of chem-

icals, as well as to foods, drugs, caffeine, and alcohol. These intolerances manifest as multisystem symptoms that frequently involve the central nervous system and often develop following a well-defined exposure event, such as home remodeling or extermination. This disease process has been called “toxicant-induced loss of tolerance.” Some affected individuals may not recall a particular initiating exposure.<sup>36</sup> In a recent study of primary care clinic patients, 20% met the criteria for chemical intolerance but only one quarter of these individuals had been diagnosed with the condition.<sup>35</sup> Researchers from this study assert that intolerances to chemicals and/or foods are potential underlying causes for illness that are rarely identified by busy practitioners but instead must be actively sought. The underlying pathophysiology of CI/toxicant-induced loss of tolerance seems to involve genetic susceptibility as well as exposure. No studies have examined developmental outcomes of children born to women who report CI. The purpose of this study was to explore whether a mother’s CI might be related to her risk of having a child diagnosed with ASD or ADHD.

### **Methods**

#### **Study Design: Assessing CI**

The most widely used instrument for evaluating CI in adult populations is the Quick Environmental Exposure and Sensitivity Inventory (QEESI), which is both sensitive (92%) and specific (95%) for CI.<sup>37,38</sup> Researchers from various countries, including the United States, Japan, and Germany, have used the QEESI to assess CI.<sup>39–41</sup>

The QEESI consists of five self-rating scales, with 10 questions each. The four core intolerance scales include Chemical Exposures, Other Exposures, Symptoms, and Impact of Sensitivities. Each scale contains 10 items that are to be rated 0 to 10 in terms of the severity of symptoms. A fifth scale, the Masking Index, provides a measure of an individual’s ongoing exposures. The two scales most indicative of CI and used for this study are Chemical Exposures and Symptoms.<sup>37,38</sup> Refer to the Appendix for an assessment of subjects’ intolerances and symptoms.

In this case–control study mothers responded to a secure computer-based survey that included the QEESI and questions on demographics and exposure/medical histories. The survey was available on the website of Children and Adults with Attention

Deficit/Hyperactivity Disorder (CHADD), a nationally recognized ADHD organization, and was advertised through community agencies and groups involved with ASD treatment and early childhood development (eg, Easter Seals). The study was reviewed and approved by the institutional review board at the University of Texas Health Science Center at San Antonio.

Case participants were biological mothers, 18 years of age or older, reporting at least 1 child with a professional diagnosis of ASD or ADHD. Other studies have shown that parents who participate in online recruitment accurately report a diagnosis of ASD in their children.<sup>42,43</sup> Further, Daniels et al.<sup>43</sup> demonstrated a 98% concordance between parent-reported and professionally diagnosed ASD, supporting the utility of online recruitment. To confirm an ADHD diagnosis in their children, mothers responded to criteria derived from the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (DSM-IV-TR).<sup>44</sup>

Case participants were asked to help recruit controls from among friends or colleagues whose children had no professionally diagnosed neurological, behavioral, or developmental disorders. Mothers of cases were asked to share the study/contact information through E-mail or word of mouth to these friends/colleagues. These potential control recruits were directed to the website by the project coordinator. Case and control responses to the *Diagnostic and Statistical Manual of Mental Disorders* criteria for ADHD were evaluated to ensure consistency with self-report.

### **Hypothesis and Statistical Analysis**

We hypothesized that mothers with higher CI scores, as measured by the QEESI, would be more likely to report having children with ASD or ADHD. Our secondary hypothesis was that mothers of children with ASD or ADHD, compared with control mothers, would report more adverse medical events and environmental intolerances in their children.

Statistical differences in average QEESI scores between cases and controls were tested using a one-way, unbalanced analysis of variance to compare means across the three groups. The Dunnett test was used to address multiple pairwise comparisons that may contribute to the type I error rate.<sup>45</sup>  $\chi^2$  tests were used to determine whether there were significant differences in dichotomous characteristics between cases and controls. A logistic model

was used to predict the presence or absence of adverse medical events and environmental intolerances between the children serving as cases and controls. The models were adjusted for the number of comorbid conditions and mother's marital status. All tests were conducted at the  $\alpha = 0.05$  level of significance using SAS software (SAS Institute, Inc., Cary, NC).

### **Results**

Table 1 shows demographic distributions across the three groups (ASD,  $n = 282$ ; ADHD,  $n = 258$ ; controls,  $n = 154$ ). We screened the first 135 respondents for ADHD case/control accuracy using the mothers' responses to the DSM-IV-TR criteria. We found 3.7% in error; that is, they reported that their child did not have a professional diagnosis, but the child met the DSM-IV-TR criteria, or vice versa. We chose not to screen additional respondents because of the small error rate. Mother's age, education, and ethnicity; family income; and the number of children did not differ significantly across groups. Of the mothers of children with ADHD, approximately 20% fewer were married compared with mothers of children with ASD or controls ( $P < .01$ ). Mothers of children with ADHD reported significantly more comorbid conditions than mothers of children with ASD or controls. Based on these differences, subsequent analysis was adjusted for marital status and comorbid conditions.

Group comparisons of the QEESI's CI total and item scores are shown in Table 2. Both mothers of children with ASD and mothers of children with ADHD had significantly higher mean CI scores than did mothers of control. Mothers of children with ASD and ADHD, compared with mothers of control, were more intolerant of insecticides, gasoline, engine exhaust, paint or paint thinner, nail polish or hairspray, and outgassing from new materials such as carpet, shower curtains, or new car interiors. In addition, compared with mothers of controls, mothers of children with ADHD were more intolerant of tobacco smoke and perfume. Mothers of children with ASD were more sensitive to tar/asphalt.

For the total Symptoms scale score (Table 3), mothers of children with ADHD or ASD differed significantly from mothers of controls in their difficulty with thinking, concentrating, memory, and

**Table 1. Descriptive Statistics Among Mothers of Children With Autism Spectrum Disorder and Attention Deficit Hyperactivity Disorder and Control Children**

	Mothers of Children With ASD (n = 282)	Mothers of Children With ADHD (n = 258)	Mothers of Control Children (n = 154)	P Value
Mean age, years (SD)	40.0 (7.8)	40.4 (8.4)	38.8 (8.2)	.162
Education (%)				.341
High school or less	9.4	9.7	11.76	
<4 Years of college	34.5	40.3	18.5	
≥4 Years College	56.1	50.0	66.3	
Non-Hispanic white race (%)	83.8	87.9	85.7	.443
Annual income (%)				.932
<50,000	29.3	32.9	31.4	
50,000–79,000	36.3	31.4	30.7	
≥80,000	34.4	35.7	37.9	
Married (%)	87.7	68.9	80.5	.010
Children, mean no. (SD)	2.3 (1.0)	2.5 (1.2)	2.3 (1.1)	.361
Number of comorbid conditions in child (%)				.001
0	34.3	9.35	56.3	
1	18.0	46.0	36.0	
2	10.6	60.6	28.9	
≥3	11.5	88.4	0	

ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder.

mood. In addition, these mothers differed significantly from mothers of controls in problems with muscle and joint pain, aching, cramping, and stiffness, as well as problems with burning eyes, airway, breathing, and coughing.

Scores ≥40 on both the Symptoms scale and Chemical Exposure scale are highly suggestive of CI.<sup>37,38</sup> Importantly, mothers with scores ≥40 on both the Symptoms and Chemical Exposure scales were three times more likely to report having a

**Table 2. Comparison of Chemical Intolerance (Quick Environmental Exposure and Sensitivity Inventory) Scores Among the Mothers of the 3 Groups of Children**

Chemical Exposures Scale	Mothers of Children With ASD		Mothers of Children With ADHD		Mothers of Control Children	
	Mean	SD	Mean	SD	Mean	SD
Total scale score	31.37*	23.66	30.90*	22.47	23.67	21.95
Items						
Diesel/gas engine exhaust	3.24*	2.75	3.34*	2.87	2.58	2.74
Tobacco smoke	3.84	3.10	4.04*	3.17	3.26	3.05
Insecticide	3.33*	3.04	3.06*	2.90	2.37	2.66
Gasoline	2.51*	2.49	2.30*	2.51	1.72	2.34
Paint/paint thinner	3.45*	2.90	3.28*	2.87	2.48	2.66
Cleaning products	3.35	2.98	3.27	2.96	2.71	2.89
Perfumes/other fragrances	3.67	3.26	3.97*	3.31	3.14	3.17
Tar/asphalt	3.06*	2.93	2.90	2.98	2.25	2.80
Nail polish, remover, hairspray	2.46*	2.57	2.35*	2.68	1.58	2.29
Carpet, shower curtain, new car smell	2.70*	2.93	2.34*	2.61	1.63	2.44

Items are scaled from 1 to 10, then summed across items for the total score, with a total possible range from 0 to 100. The range for control mothers was 0 to 88, 1 to 92 for mothers of children with attention deficit hyperactivity disorder (ADHD), and 0 to 90 for mothers of children with autism spectrum disorder (ASD).

\* $P < .05$ .

SD, standard deviation.

**Table 3. Average Quick Environmental Exposure and Sensitivity Inventory Symptoms Scores for Mothers of Cases and Controls**

	Mothers of Children With ASD		Mothers of Children With ADHD		Mothers of Control Children	
	Mean	SD	Mean	SD	Mean	SD
Total scale score	31.67*	21.86	32.92*	21.04	23.53	20.94
Items						
Problems with muscles, joints, such as pain, aching, cramping, stiffness	3.19*	3.12	3.02*	3.00	2.21	2.86
Problems with burning eyes, airway, breathing, coughing	2.88*	3.07	2.80*	3.05	2.02	2.80
Problems with heart or chest	2.32*	2.84	1.75	2.62	1.26	2.01
Problems with stomach or digestive tract	3.25	3.05	3.31*	3.12	2.57	2.99
Problems with ability to think, difficulty concentrating, remembering	3.58*	3.05	4.47*	3.43	2.51	2.98
Problems with mood, tense or nervous, depressed	3.99*	3.07	4.83*	3.28	3.25	3.16
Problems with balance, numbness in extremities	2.47	2.82	2.55	3.05	1.93	2.84
Problems with head or face	4.01	3.11	4.71*	3.44	3.48	3.01
Problems with skin, rash, hives	3.12*	3.02	2.79	2.95	2.19	2.81
Problems with urinary tract or frequent urination	2.93*	3.04	2.64	3.18	2.17	2.79

Items are scaled from 1 to 10, then summed across items for the total score, with a total possible range from 0 to 100. The range for mothers of control children was 0 to 83, 1 to 93 for mothers of children with attention deficit hyperactivity disorder (ADHD), and 0 to 95 for mothers of children with autism spectrum disorder (ASD).

\* $P < .05$ .

SD, standard deviation.

child with ASD (odds ratio [OR], 3.01; 95% confidence interval [CI], 1.50–6.02). Similarly, for ADHD, mothers whose scores were  $\geq 40$  on both the Symptoms and Chemical Exposure scales were 2.3 times more likely to report having a child with ADHD (OR, 2.3; 95% CI, 1.12–5.04). To determine whether the Symptoms scale was potentially driven by two behavioral items commonly found in families with ADHD (problems with ability to think, difficulty concentrating, remembering; problems with mood, tense or nervous, depressed), these items were removed from the scale and the responses were reanalyzed. The results were the same and did not change the interpretation presented above.

Notably, the significant distinguishing items between mothers of cases (both ASD and ADHD) and controls on the Other Exposures scale was the inability to tolerate certain drugs or having had adverse drug reactions ( $P < .01$ ) and problems with classic allergic reactions when exposed to allergens ( $P < .05$ ; data not shown).

In Table 4, children's medical and intolerance outcomes are predicted by their ASD or ADHD status. Compared with control children, children

with ASD or ADHD were, according to their mothers, significantly more likely to have sensitivities to odors, problems with allergies, and strong food preferences or cravings. Compared with mothers of controls, mothers of children with ASD were statistically more likely to report that their children had food or other allergies/intolerances; an adverse reaction to a vaccination, prompting a call to the doctor; ear infections requiring tube placement; and multiple infections requiring prolonged use of antibiotics.

## Discussion

Our results suggest that mothers with CI are more likely to have children with ASD or ADHD than mothers without CI. Compared with controls, mothers with CI from our study report more cognitive and affective symptoms, consistent with the broader literature showing increased cognitive and mood disorders among families with children with ASD and ADHD.<sup>46,47</sup>

Notably, compared with mothers of controls, mothers of children with ASD or ADHD were significantly more likely to report that their chil-



**Table 4. Mother's Report of Their Children's Illnesses or Responses to Common Exposures**

Reported Illnesses or Responses to Exposures	Children With ADHD			Children With ASD		
	OR	95% CI	<i>P</i> Value*	OR	95% CI	<i>P</i> Value*
Reactions to vaccinations that prompted a call to the doctor	0.75	0.32–1.7	.484	<b>3.7</b>	1.8–7.5	<b>&lt;.001</b>
Ear infections requiring tubes placed in the ears	1.4	0.8–2.2	.242	<b>1.7</b>	<b>1.1–2.7</b>	<b>.020</b>
Multiple infections requiring prolonged use of antibiotics	1.74	0.9–3.2	.072	<b>4.9</b>	<b>2.7–8.6</b>	<b>&lt;.001</b>
Sensitivity to odors such as smoke, nail polish remover, exhaust, gasoline, air fresheners, or cleaning supplies. By sensitive we mean, does this child become nauseated, get headaches, have trouble breathing, feel dizzy, or try to move away from the odor?	<b>2.00</b>	<b>1.1–4.0</b>	<b>.041</b>	<b>3.5</b>	<b>1.9–6.8</b>	<b>&lt;.001</b>
Exhibited food allergies or intolerances	1.07	0.6–1.8	.790	<b>3.3</b>	<b>2.1–5.1</b>	<b>&lt;.001</b>
Strong food preferences/cravings such as cheese, chips, bread, pasta, rice, sugar, salt, and chocolate	<b>2.00</b>	1.3–3.1	<b>.003</b>	<b>4.8</b>	<b>3.2–7.5</b>	<b>&lt;.001</b>
Became sick from an environmental exposure	0.49	0.12–2.1	.320	2.2	0.77–7.8	.176
Allergies	<b>2.00</b>	1.3–3.1	<b>.002</b>	<b>1.6</b>	<b>1.1–2.4</b>	<b>.020</b>
Asthma	1.1	0.6–1.6	.980	1.38	0.82–2.2	.250

Analysis was adjusted for marital status and comorbid conditions.

\**P* values compare cases to controls. Bold values indicate statistical significance.

ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; CI, confidence interval; OR, odds ratio.

dren were especially sensitive to a wide range of chemical odors—the hallmark symptom of CI. These mothers also were significantly more likely to report that their children have problems with allergies, sensitivities, infections, reactions to drugs (oral or injected), and/or foods than mothers of neurotypical children. The recent literature supports comorbid allergies and food cravings/sensitivities in both children with ASD and children with ADHD.<sup>48–50</sup> Neurodevelopmental comorbidities in children with ASD and children with ADHD are the norm rather than the exception; therefore, eliminating children on this basis would not be feasible. Medical comorbidities also are common among children with these disorders. In our sample, for both ASD and ADHD these comorbidities included mental retardation, anxiety, epilepsy, auditory and visual processing disorders, depression, and obsessive compulsive disorders.

Our findings are consistent with our hypothesis that mothers with CI are more apt to have children with similar intolerances. Children who inherit their mothers' susceptibilities may be at greater risk from exposure to toxicants, either in utero or after birth.

We tested mothers' current CI, which does not tell us whether she had it before pregnancy; it simply tells us that she may be more vulnerable to toxins. Although this study is neither a genetic study nor a prospective chemical exposure study,

our data may suggest that children inherit these susceptibilities and intolerances. Increased nitrite/nitrate and inflammatory cytokine levels as well as genetic polymorphisms in detoxification enzymes have recently been implicated in CI.<sup>51</sup> One well-understood example of mothers conferring susceptibility to environmental chemicals involves pesticide exposure. Mothers who are less able to detoxify organophosphorus pesticides because of low paraoxonase enzyme activity are at increased risk for having children with ASD and ADHD.<sup>52,53</sup> Studies by Singh et al<sup>54,55</sup> provide evidence that individuals with more susceptible genotypes who are exposed to organophosphorus pesticides exhibit greater DNA damage. Thus, “dose plus host” determines toxicity.

Primary care physicians may be first in line to recognize and refer a child with symptoms of ADHD or ASD. Thus, it is important for them to develop practical plans for screening and referral. Because of the many comorbid health conditions associated with ASD and ADHD, these children and their families have many unmet medical needs.<sup>5,7,9</sup> The availability of a medical home for family care may reduce these burdens.<sup>7</sup> Future medical homes need to address the family's *actual* home environment. For doctors in already overburdened practices, taking time to obtain an exposure history and discuss environmental interventions may seem overwhelm-

ing. Primary care physicians could, however, offer Table 5 as a preconception precautionary tool, since roughly one third of pregnant women reported seeing a primary care physician within the previous year.<sup>56</sup>

In the recent past, doctors were hesitant to advise women to avoid alcohol and tobacco during pregnancy for fear of making the mothers feel guilty or worried about their pregnancy, even though there was sufficient evidence to do so. The American College of Obstetricians and Gynecologists recently issued a position statement recommending timely action to reduce additional exposures: “The evidence that links exposure to toxic environmental agents and adverse reproductive and developmental health outcomes is sufficiently robust. . . .”<sup>57</sup> Home environmental interventions to help children with ASD or ADHD could have the dual benefit of reducing exposures that may be affecting the health of other family members. Asthma and migraines can be exacerbated by tobacco smoke, pesticides, new construction/remodeling, and fragrances. Recommendations in Table 5 may reduce symptoms of asthma and other environmentally related illnesses and can encourage families to share responsibility for their own health.

Families are most receptive to making major lifestyle changes, such as reducing smoking and chemical use, when they are expecting a new arrival. This is consistent with the applications of the precautionary principle in public health, which indicates that if there is potential threat of harm to human or environmental health, precautionary

measures should be taken to avoid the threat even before there is scientific consensus concerning cause and effect. This implies that there is a social responsibility to protect the public from harm when a plausible risk is present.

### Limitations

These data are cross-sectional, and causal mechanisms cannot be inferred because of confounders in this limited sample. Ours was a large, self-selected convenience sample (n = 694) mainly consisting of non-Hispanic white, educated women responding to an online survey. Our sample demographics are consistent with those of other online studies.<sup>58</sup> While the “digital divide” between affluent and nonaffluent people is slowly closing over time,<sup>59</sup> we cannot verify a representative sample, and therefore these results must be generalized to other populations with caution. Self-selection is based on a willingness to participate, and mothers with an affected child would be more willing than those with an unaffected child, adding potential sampling biases. Mothers of children with ASD or ADHD may be more attuned to searching for causes for their child’s condition,<sup>60</sup> potentially resulting in overreporting of exposures compared with controls. Fewer friend/colleague controls were recruited than cases. Further, the lower response rate from control mothers may be the result of less interest in the study outcome because their children are neurotypical and they are not intrinsically motivated to learn about what may contribute to autism or ADHD. Therefore, this study may not be consid-

**Table 5. Recommendations for Reducing Exposures**

Instead of Using . . .	Try Using . . .
Pesticides indoors or on lawns; mothballs	Baits or traps to control bugs indoors (avoid attracting bugs by tightly sealing foods, including pet foods)
Paints, varnishes, glues, and polishes with high solvent content	Paints with low solvent content, water-based finishes and glues (have these applied when you are away from home)
Bleach, ammonia, disinfectants, and strong cleaning products	“Elbow grease,” soap and water, baking soda and vinegar
Scented products, perfumes, air fresheners, and incense	Unscented cleansers, laundry detergent, fabric softeners, and cosmetics; organic essential oils
Hair coloring, permanents, hair spray, or any aerosol product	New haircut and unscented hair gel or styling products that do not require spraying
Dry cleaning, odorous soft plastic toys, or mattress covers	Washable toys, bedding, and clothes
Odorous flooring (eg, vinyl, pressed wood, or particle board) or carpeting, which can also trap allergens	Ceramic/stone tile or hardwood floors
Commercial foods/beverages that may contain pesticides or other questionable ingredients	Organic foods and foods without additives or artificial colors
Plastic food containers	Glass, stainless steel containers

ered a rigorous case-control study because the recruitment of cases and controls have inherent biases affecting generalizability.<sup>61</sup> The extent to which these biases affect our results is unknown; therefore, more rigorous epidemiologic studies are needed to verify the results of this study.

## Conclusion

These data provide preliminary evidence for an association between maternal CI and risk of ASD and ADHD in children. Further studies are needed to confirm these findings. We are dealing with a public health emergency with the increase in neurodevelopmental disorders, however, and it is incumbent on us to take appropriate preventive steps. Establishing clear cause-and-effect relationships between neurodevelopmental disorders and exposures may require decades of costly epidemiologic studies. In the meantime, primary care physicians should advocate a precautionary approach, as recommended by the American College of Obstetricians and Gynecologists, to encourage women of childbearing age to avoid unnecessary exposures.<sup>57</sup>

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## Appendix

### ***The Quick Environmental Exposure and Sensitivity Inventory***

The QEESI is a validated instrument to assess CI in adults.<sup>37,38</sup> The QEESI consists of self-rating scales for symptoms, as well as responses to chemical and other common exposures, including foods, skin contactants, alcoholic beverages, and caffeine. Each of these three scales (Symptoms, Chemical Exposures, and Other Exposures) contains 10 items that participants rate from 0 to 10 in terms of the severity of their responses. The development, validation, sensitivity, and specificity of these scales are published elsewhere.<sup>37,38,62</sup>

#### *Symptoms Scale*

The Symptoms scale includes head-related, musculo-skeletal, respiratory/mucus membrane, heart/chest, neuromuscular, gastrointestinal, cognitive, affective, skin, and genitourinary symptoms. Scoring for this scale is accomplished by asking participants to

rate each item from 0 to 10 in a manner that best corresponds with the severity of their symptoms and responses to various substances: 0 = not a problem, 5 = moderate, 10 = severe or disabling. Scores on the 10 items for each scale are tallied to obtain a total scale score (0–100).

#### *Chemical Exposures Scale*

This scale asks participants about the severity of their responses to 10 common structurally diverse inhalants, rated from 0 to 10, as described above. Items include diesel or gas engine exhaust, tobacco smoke, insecticide, gasoline vapors, paint/paint thinner, fragrances, cleaning products, fresh tar or asphalt, nail polish/nail polish remover, hairspray, and new furnishings.

#### *Other Exposures Scale*

The Other Exposures scale includes 10 additional questions concerning the severity of the subjects’ responses to a variety of other common exposures (noninhalants), again asking them to rate their response severity from 0 to 10. These items include chlorinated tap water, foods/food additives, unusual cravings or feeling ill if a meal is missed, feeling ill after meals, caffeine, caffeine withdrawal, small amounts of alcoholic beverages, skin contactants, medical drugs/devices, and allergens (causing classic allergic responses of asthma, nasal symptoms, hives, eczema, or anaphylaxis).

### ***Mother’s Report of Children’s Illnesses and Responses to Exposures***

Each mother was asked about her child’s sensitivities and responses to various common exposures. Included were questions concerning (1) reactions to vaccinations that prompted a call to the doctor; (2) ear infections requiring tubes placed in the ears; (3) multiple infections requiring prolonged use of antibiotics; (4) sensitivity to odors such as smoke, nail polish remover, exhaust, gasoline, air fresheners, or cleaning supplies (by sensitive, we mean does this child become nauseated, get headaches, have trouble breathing, feel dizzy, or try to move away from the odor); (5) food allergies or intolerances; (6) strong food preferences/cravings such as cheese, chips, bread, pasta, rice, sugar, salt, chocolate; (7) illness following an environmental exposure; (8) allergies; and (9) asthma. See <http://drclaudiamiller.com/neesitest/> for printable copy for use in your practice.