

## Neurodevelopmental Disorders

Neurodevelopmental disorders are disabilities associated primarily with the functioning of the neurological system and brain. Examples of neurodevelopmental disorders in children include attention-deficit/hyperactivity disorder (ADHD), autism, learning disabilities, intellectual disability (also known as mental retardation), conduct disorders, cerebral palsy, and impairments in vision and hearing. Children with neurodevelopmental disorders can experience difficulties with language and speech, motor skills, behavior, memory, learning, or other neurological functions. While the symptoms and behaviors of neurodevelopmental disabilities often change or evolve as a child grows older, some disabilities are permanent. Diagnosis and treatment of these disorders can be difficult; treatment often involves a combination of professional therapy, pharmaceuticals, and home- and school-based programs.

Based on parental responses to survey questions, approximately 15% of children in the United States ages 3 to 17 years were affected by neurodevelopmental disorders, including ADHD, learning disabilities, intellectual disability, cerebral palsy, autism, seizures, stuttering or stammering, moderate to profound hearing loss, blindness, and other developmental delays, in 2006–2008.<sup>1</sup> Among these conditions, ADHD and learning disabilities had the greatest prevalence. Many children affected by neurodevelopmental disorders have more than one of these conditions: for example, about 4% of U.S. children have both ADHD and a learning disability.<sup>2</sup> Some researchers have stated that the prevalence of certain neurodevelopmental disorders, specifically autism and ADHD, has been increasing over the last four decades.<sup>3–7</sup> Long-term trends in these conditions are difficult to detect with certainty, due to a lack of data to track prevalence over many years as well as changes in awareness and diagnostic criteria. However, some detailed reviews of historical data have concluded that the actual prevalence of autism seems to be rising.<sup>4,8–10</sup> Surveys of educators and pediatricians have reported a rise in the number of children seen in classrooms and exam rooms with behavioral and learning disorders.<sup>11–13</sup>

Genetics can play an important role in many neurodevelopmental disorders, and some cases of certain conditions such as intellectual disability are associated with specific genes. However, most neurodevelopmental disorders have complex and multiple contributors rather than any one clear cause. These disorders likely result from a combination of genetic, biological, psychosocial and environmental risk factors. A broad range of environmental risk factors may affect neurodevelopment, including (but not limited to) maternal use of alcohol, tobacco, or illicit drugs during pregnancy; lower socioeconomic status; preterm birth; low birthweight; the physical environment; and prenatal or childhood exposure to certain environmental contaminants.<sup>14–21</sup>

Lead, methylmercury, and PCBs are widespread environmental contaminants associated with adverse effects on a child's developing brain and nervous system in multiple studies. The National Toxicology Program (NTP) has concluded that childhood lead exposure is associated

with reduced cognitive function, including lower intelligence quotient (IQ) and reduced academic achievement.<sup>22</sup> The NTP has also concluded that childhood lead exposure is associated with attention-related behavioral problems (including inattention, hyperactivity, and diagnosed attention-deficit/hyperactivity disorder) and increased incidence of problem behaviors (including delinquent, criminal, or antisocial behavior).<sup>22</sup>

EPA has determined that methylmercury is known to have neurotoxic and developmental effects in humans.<sup>23</sup> Extreme cases of such effects were seen in people prenatally exposed during two high-dose mercury poisoning events in Japan and Iraq, who experienced severe adverse health effects such as cerebral palsy, mental retardation, deafness, and blindness.<sup>24-26</sup> Prospective cohort studies have been conducted in island populations where frequent fish consumption leads to methylmercury exposure in pregnant women at levels much lower than in the poisoning incidents but much greater than those typically observed in the United States. Results from such studies in New Zealand and the Faroe Islands suggest that increased prenatal mercury exposure due to maternal fish consumption was associated with adverse effects on intelligence and decreased functioning in the areas of language, attention, and memory.<sup>26-32</sup> These associations were not seen in initial results reported from a similar study in the Seychelles Islands.<sup>33</sup> However, further studies in the Seychelles found associations between prenatal mercury exposure and some neurodevelopmental deficits after researchers had accounted for the developmental benefits of fish consumption.<sup>34-36</sup> More recent studies conducted in the United States have found associations between neurodevelopmental effects and blood mercury levels within the range typical for U.S. women, after accounting for the beneficial effects of fish consumption during pregnancy.<sup>32,37,38</sup>

Several studies of children who were prenatally exposed to elevated levels of polychlorinated biphenyls (PCBs) have suggested linkages between these contaminants and neurodevelopmental effects, including lowered intelligence and behavioral deficits such as inattention and impulsive behavior.<sup>39-44</sup> Studies have also reported associations between PCB exposure and deficits in learning and memory.<sup>39,45</sup> Most of these studies found that the effects are associated with exposure in the womb resulting from the mother having eaten food contaminated with PCBs,<sup>46-51</sup> although some studies have reported relationships between adverse effects and PCB exposure during infancy and childhood.<sup>45,51-53</sup> Although there is some inconsistency in the epidemiological literature, several reviews of the literature have found that the overall evidence supports a concern for effects of PCBs on children's neurological development.<sup>52,54-58</sup> The Agency for Toxic Substances and Disease Registry has determined that "Substantial data suggest that PCBs play a role in neurobehavioral alterations observed in newborns and young children of women with PCB burdens near background levels."<sup>59</sup> In addition, adverse effects on intelligence and behavior have been found in children of women who were highly exposed to mixtures of PCBs, chlorinated dibenzofurans, and other pollutants prior to conception.<sup>60-63</sup>

A wide variety of other environmental chemicals have been identified as potential concerns for childhood neurological development, but have not been as well studied for these effects as lead, mercury, and PCBs. Concerns for these additional chemicals are based on both laboratory

animal studies and human epidemiological research; in most cases, the epidemiological studies are relatively new and the literature is just beginning to develop. Among the chemicals being studied for potential effects on childhood neurological development are organophosphate pesticides, polybrominated diphenyl ether flame retardants (PBDEs), phthalates, bisphenol A (BPA), polycyclic aromatic hydrocarbons (PAHs), arsenic, and perchlorate. Exposure to all of these chemicals is widespread in the United States for both children and adults.<sup>64</sup>

Organophosphate pesticides can interfere with the proper function of the nervous system when exposure is sufficiently high.<sup>65</sup> Many children may have low capacity to detoxify organophosphate pesticides through age 7 years.<sup>66</sup> In addition, recent studies have reported an association between prenatal organophosphate exposure and childhood ADHD in a U.S. community with relatively high exposures to organophosphate pesticides,<sup>67</sup> as well as with exposures found within the general U.S. population.<sup>68</sup> Other recent studies have described associations between prenatal organophosphate pesticide exposures and a variety of neurodevelopmental deficits in childhood, including reduced IQ, perceptual reasoning, and memory.<sup>69-71</sup>

Studies of certain PBDEs have found adverse effects on behavior, learning, and memory in laboratory animals.<sup>72-74</sup> A recent epidemiological study in New York City reported significant associations between children's prenatal exposure to PBDEs and reduced performance on IQ tests and other tests of neurological development in 6-year-old children.<sup>75</sup> Another study in the Netherlands reported significant associations between children's prenatal exposure to PBDEs and reduced performance on some neurodevelopmental tests in 5- and 6-year-old children, while associations with improved performance were observed for other tests.<sup>76</sup>

Two studies of a group of New York City children ages 4 to 9 years reported associations between prenatal exposure to certain phthalates and behavioral deficits, including effects on attention, conduct, and social behaviors.<sup>77,78</sup> Some of the behavioral deficits observed in these studies are similar to those commonly displayed in children with ADHD and conduct disorder. Studies conducted in South Korea of children ages 8 to 11 years reported that children with higher levels of certain phthalate metabolites in their urine were more inattentive and hyperactive, displayed more symptoms of ADHD, and had lower IQ compared with those who had lower levels.<sup>79,80</sup> The exposure levels in these studies are comparable to typical exposures in the U.S. population.

In 2008, the NTP concluded that there is "some concern" for effects of early-life (including prenatal) BPA exposure on brain development and behavior, based on findings of animal studies conducted at relatively low doses.<sup>81</sup> An epidemiological study conducted in Ohio reported an association between prenatal exposure to BPA and effects on children's behavior (increased hyperactivity and aggression) at age 2 years.<sup>82</sup> Another study of prenatal BPA exposure in New York City reported no association between prenatal BPA exposure and social behavior deficits in testing conducted at ages 7 to 9 years.<sup>78</sup>

A series of recent studies conducted in New York City has reported that children of women who were exposed to increased levels of polycyclic aromatic hydrocarbons (PAHs, produced when

gasoline and other materials are burned) during pregnancy are more likely to have experienced adverse effects on neurological development (for example, reduced IQ and behavioral problems).<sup>83,84</sup>

Early-life exposure to arsenic has been associated with measures of reduced cognitive function, including lower scores on tests that measure neurobehavioral and intellectual development, in four studies conducted in Asia; however there are some inconsistencies in the findings of these studies.<sup>85</sup> These findings are from countries where arsenic levels in drinking water are generally much higher than in the United States due to high levels of naturally occurring arsenic in groundwater.<sup>86</sup>

Perchlorate is a naturally occurring and man-made chemical that has been found in drinking water<sup>87</sup> and foods<sup>88,89</sup> in the United States. Exposure to elevated levels of perchlorate inhibits iodide uptake into the thyroid gland, thus possibly disrupting the function of the thyroid and potentially leading to a reduction in the production of thyroid hormone.<sup>90,91</sup> Moderate deficits in maternal thyroid hormone levels during early pregnancy have been linked to reduced childhood IQ scores and other neurodevelopmental effects.<sup>92-94</sup>

Interactions of environmental contaminants and other environmental factors may combine to increase the risk of neurodevelopmental disorders. For example, exposure to lead may have stronger effects on neurodevelopment among children with lower socioeconomic status.<sup>21,95</sup>

A child's brain and nervous system are vulnerable to adverse impacts from pollutants because they go through a long developmental process beginning shortly after conception and continuing through adolescence.<sup>96,97</sup> This complex developmental process requires the precise coordination of cell growth and movement, and may be disrupted by even short-term exposures to environmental contaminants if they occur at critical stages of development. This disruption can lead to neurodevelopmental deficits that may have an effect on the child's achievements and behavior even when they do not result in a diagnosable disorder.

## Attention-Deficit/Hyperactivity Disorder (ADHD)

Attention-deficit/hyperactivity disorder (ADHD) is a disruptive behavior disorder characterized by symptoms of inattention and/or hyperactivity-impulsivity, occurring in several settings and more frequently and severely than is typical for other individuals in the same stage of development.<sup>98</sup> ADHD can make family and peer relationships difficult, diminish academic performance, and reduce vocational achievement.

As the medical profession has developed a greater understanding of ADHD through the years, the name of this condition has changed. The American Psychiatric Association adopted the name "attention deficit disorder" in the early 1980s and revised it to "attention-deficit/hyperactivity disorder" in 1987.<sup>99</sup> Many children with ADHD have a mix of inattention and hyperactivity/impulsivity behaviors, while some may display primarily hyperactive behavior traits, and others display primarily inattentive traits. It is possible for an individual's primary

symptoms of ADHD to change over time.<sup>20</sup> Children with ADHD frequently have other disorders, with parents reporting that about half of children with ADHD have a learning disability and about one in four have a conduct disorder.<sup>2,100</sup>

Other disorders, including anxiety disorders, depression, and learning disabilities, can be expressed with signs and symptoms that resemble those of ADHD. A diagnosis of ADHD requires a certain amount of judgment on the part of a doctor, similar to diagnosis of other mental disorders. Despite the variability among children diagnosed with the disorder and the challenges involved in diagnosis, ADHD has good clinical validity, meaning that impaired children share similarities, exhibit symptoms, respond to treatment, and are recognized with general consistency across clinicians.<sup>20</sup>

A great deal of research on ADHD has focused on aspects of brain functioning that are related to the behaviors associated with ADHD. Although this research is not definitive, it has found that children with ADHD generally have trouble with certain skills involved in problem-solving (referred to collectively as executive function). These skills include working memory (keeping information in mind while briefly doing something else), planning (organizing a sequence of activities to complete a task), response inhibition (suppressing immediate responses when they are inappropriate), and cognitive flexibility (changing an approach when a situation changes). Children with ADHD also generally have problems in maintaining sustained attention to a task (referred to as vigilance), and/or maintaining readiness to respond to new information (referred to as alertness).<sup>20,101,102</sup>

While uncertainties remain, findings to date indicate that ADHD is caused by combinations of genetic and environmental factors.<sup>20,103-106</sup> Much of the research on environmental factors has focused on the fetal environment. Maternal smoking during pregnancy has been associated with increased risk of ADHD in the child in numerous studies, however, this continues to be an active area of research as scientists consider whether other factors related to smoking (e.g., genetic factors, maternal mental health, stress, alcohol use, and low birth weight) may be responsible for associations attributed to smoking.<sup>17,19,107</sup> Findings regarding ADHD and maternal consumption of alcohol during pregnancy are considered more limited and inconsistent.<sup>19,20</sup> Preterm birth and low birth weight have also been found to increase the likelihood that a child will have ADHD.<sup>16,18,20</sup> Psychosocial adversity (representing factors such as low socioeconomic status and in-home conflict) in childhood may also play a role in ADHD.<sup>108</sup>

The potential role of environmental contaminants in contributing to ADHD, either alone or in conjunction with certain genetic susceptibilities or other environmental factors, is becoming better understood as a growing number of studies look explicitly at the relationship between ADHD and exposures to environmental contaminants.

Among environmental contaminants known or suspected to be developmental neurotoxicants, lead has the most extensive evidence of a potential contribution to ADHD. A number of recent epidemiological studies (all published since 2006, with data gathered beginning in 1999 or more recently) conducted in the United States and Asia have reported relationships between

increased levels of lead in a child's blood and increased likelihood of ADHD.<sup>55,109-115</sup> In most of these studies, blood lead levels were comparable to levels observed currently in the United States. The potential contribution of childhood lead exposure to the risk of ADHD may be amplified in children of women who smoked cigarettes during pregnancy.<sup>110</sup> In addition, several studies have reported relationships between blood lead levels and the aspects of brain functioning that are most affected in children with ADHD, including sustained attention, alertness, and problem-solving skills (executive functions, specifically cognitive flexibility, working memory, planning, and response inhibition).<sup>22,44,55,116-119</sup> Similar results have been observed in laboratory animal studies.<sup>55,96,120-122</sup> The NTP has concluded that childhood lead exposure is "associated with increased diagnosis of attention-related behavioral problems."<sup>22</sup>

Although no studies evaluating a potential association between PCBs and ADHD itself have been published, a study in Massachusetts reported a relationship between levels of PCBs measured in cord blood and increased ADHD-like behaviors observed by teachers in children at ages 7 to 11 years. PCB levels in this study were generally lower than those measured in other epidemiological studies of PCBs and childhood neurological development.<sup>40</sup> Other research findings also suggest that PCBs may play a role in contributing to ADHD. Several studies in U.S. and European populations, most having elevated exposure to PCBs through the diet, have found generally consistent associations with aspects of brain function that are most affected in children with ADHD, including alertness and problem-solving skills (executive functions, specifically response inhibition, working memory, cognitive flexibility, and planning).<sup>54,55</sup> Studies in laboratory animals have similar findings regarding the mental functions affected by PCB exposure.<sup>55,96</sup>

Studies of other environmental chemicals reporting associations with ADHD or related outcomes have been published in recent years, but findings tend to be much more limited than for lead and PCBs. Findings for phthalates and organophosphate pesticides were noted above. In addition, three studies have reported associations between ADHD or impulsivity and concentrations of certain perfluorinated chemicals measured in the blood of children.<sup>123-125</sup> Studies of mercury have produced generally mixed findings of associations with ADHD or related symptoms and mental functions.<sup>29,111,118,126-128</sup>

## Learning Disability

Learning disability (or learning disorder) is a general term for a neurological disorder that affects the way in which a child's brain can receive, process, retain, and respond to information. A child with a learning disability may have trouble learning and using certain skills, including reading, writing, listening, speaking, reasoning, and doing math, although learning disabilities vary from child to child. Children with learning disabilities usually have average or above-average intelligence, but there are differences in the way their brains process information.<sup>129</sup>

As with many other neurodevelopmental disorders, the causes of learning disabilities are not well understood. Often learning disabilities run in the family, suggesting that heredity may play a role in their development. Problems during pregnancy and birth, such as drug or alcohol use

during pregnancy, low birth weight, lack of oxygen, or premature or prolonged labor, may also lead to learning disabilities.<sup>130</sup>

As is the case with other neurodevelopmental outcomes, there are generally many more studies of lead exposure that are relevant to learning disabilities than for other environmental contaminants. Several studies have found associations between lead exposure and learning disabilities or reduced classroom performance that are independent of IQ.<sup>119,120,131-133</sup> Exposures to lead have been associated with impaired memory and difficulties or impairments in rule learning, following directions, planning, verbal abilities, speech processing, and classroom performance in children.<sup>22,119,131,134-137</sup> Other findings that may indicate contributions from environmental contaminants to learning disabilities include a study that found associations of both maternal smoking during pregnancy and childhood exposure to environmental tobacco smoke with parent report of a child with a learning disability diagnosis;<sup>138</sup> associations of prenatal mercury exposure with dysfunctions in children's language abilities and memory,<sup>29,30</sup> and associations of prenatal PCB exposure with poorer concentration and memory deficits compared with unexposed children.<sup>39,45</sup>

### Autism Spectrum Disorders

Autism spectrum disorders (ASDs) are a group of developmental disabilities defined by significant social, communication, and behavioral impairments. The term “spectrum disorders” refers to the fact that although people with ASDs share some common symptoms, ASDs affect different people in different ways, with some experiencing very mild symptoms and others experiencing severe symptoms. ASDs encompass autistic disorder and the generally less severe forms, Asperger's syndrome and pervasive developmental disorder-not otherwise specified (PDD-NOS). Children with ASDs may lack interest in other people, have trouble showing or talking about feelings, and avoid or resist physical contact. A range of communication problems are seen in children with ASDs: some speak very well, while many children with an ASD do not speak at all. Another hallmark characteristic of ASDs is the demonstration of restrictive or repetitive interests or behaviors, such as lining up toys, flapping hands, rocking his or her body, or spinning in circles.<sup>139</sup>

To date, no single risk factor sufficient to cause ASD has been identified; rather each case is likely to be caused by the combination of multiple genetic and environmental risk factors.<sup>140-142</sup> Several ASD research findings and hypotheses may imply an important role for environmental contaminants. First, there has been a sharp upward trend in reported prevalence that cannot be fully explained by factors such as younger ages at diagnosis, migration patterns, changes in diagnostic criteria, inclusion of milder cases, or increased parental age.<sup>8,9,143-146</sup> Also, the neurological signaling systems that are impaired in children with ASDs can be affected by certain environmental chemicals. For example, several pesticides are known to interfere with acetylcholine (ACh) and  $\gamma$ -aminobutyric acid (GABA) neurotransmission, chemical messenger systems that have been altered in certain subsets of autistic individuals.<sup>147</sup> Some studies have reported associations between certain

pharmaceuticals taken by pregnant women and increased incidence of autism, which may suggest that there are biological pathways by which other chemical exposures during pregnancy could increase the risk of autism.<sup>148</sup>

Furthermore, some of the identified genetic risk factors for autism are *de novo* mutations, meaning that the genetic defect is not present in either of the parents' genes, yet can be found in the genes of the child when a new genetic mutation forms in a parent's germ cells (egg or sperm), potentially from exposure to contaminants.<sup>140,142,149,150</sup> Many environmental contaminants have been identified as agents capable of causing mutations in DNA, by leading to oxidative DNA damage and by inhibiting the body's normal ability to repair DNA damage.<sup>151</sup> Some children with autism have been shown to display markers of increased oxidative stress, which may strengthen this line of reasoning.<sup>152-154</sup> Many studies have linked increasing paternal and maternal age with increased risk of ASDs.<sup>144,146,155-157</sup> The role of parental age in increased autism risk might be explained by evidence that shows advanced parental age can contribute significantly to the frequency of *de novo* mutations in a parent's germ cells.<sup>151,158,159</sup> Advanced parental age signifies a longer period of time when environmental exposures may act on germ cells and cause DNA damage and *de novo* mutations. Finally, a recent study concluded that the role of genetic factors in ASDs has been overestimated, and that environmental factors play a greater role than genetic factors in contributing to autism.<sup>141</sup> This study did not evaluate the role of any particular environmental factors, and in this context "environmental factors" are defined broadly to include any influence that is not genetic.

Studies, limited in number and often limited in research design, have examined the possible role that certain environmental contaminants may play in the development of ASDs. A number of these studies have focused on mercury exposures. Earlier studies reported higher levels of mercury in the blood, baby teeth, and urine of children with ASDs compared with control children;<sup>160-162</sup> however, another more recent study reported no difference in the blood mercury levels of children with autism and typically developing children.<sup>163</sup> Proximity to industrial and power plant sources of environmental mercury was reported to be associated with increased autism prevalence in a study conducted in Texas.<sup>164</sup>

Thimerosal is a mercury-containing preservative that is used in some vaccines to prevent contamination and growth of harmful bacteria in vaccine vials. Since 2001, thimerosal has not been used in routinely administered childhood vaccines, with the exception of some influenza vaccines.<sup>165</sup> The Institute of Medicine has rejected the hypothesis of a causal relationship between thimerosal-containing vaccines and autism.<sup>166</sup>

Some studies have also considered air pollutants as possible contributors to autism. A study conducted in the San Francisco Bay Area reported an association between the amount of certain airborne pollutants at a child's place of birth (mercury, cadmium, nickel, trichloroethylene, and vinyl chloride) and the risk for autism, but a similar study in North Carolina and West Virginia did not find such a relationship.<sup>167,168</sup> Another study in California reported that mothers who lived near a freeway at the time of delivery were more likely to



have children diagnosed with autism, suggesting that exposure to traffic-related air pollutants may play a role in contributing to ASDs.<sup>169</sup>

Finally, a study in Sweden reported an increased risk of ASDs in children born to families living in homes with polyvinyl chloride (PVC) flooring, which is a source of certain phthalates in indoor environments.<sup>170</sup>

## Intellectual Disability (Mental Retardation)

The most commonly used definitions of intellectual disability (also referred to as mental retardation) emphasize subaverage intellectual functioning before the age of 18, usually defined as an IQ less than 70 and impairments in life skills such as communication, self-care, home living, and social or interpersonal skills. Different severity categories, ranging from mild to severe retardation, are defined on the basis of IQ scores.<sup>171,172</sup>

“Intellectual disability” is used as the preferred term for this condition in the disabilities sector, but the term “mental retardation” continues to be used in the contexts of law and public policy when designating eligibility for state and federal programs.<sup>171</sup>

Researchers have identified some causes of intellectual disability, including genetic disorders, traumatic injuries, and prenatal events such as maternal infection or exposure to alcohol.<sup>172,173</sup> However, the causes of intellectual disability are unknown in 30–50% of all cases.<sup>173</sup> The causes are more frequently identified for cases of severe retardation (IQ less than 50), whereas the cause of mild retardation (IQ between 50 and 70) is unknown in more than 75% of cases.<sup>174,175</sup> Exposures to environmental contaminants could be a contributing factor to the cases of mild retardation where the cause is unknown. Exposure to high levels of lead and mercury have been associated with intellectual disability.<sup>23,176-178</sup> Furthermore, lead, mercury, and PCBs all have been found to have adverse effects on intelligence and cognitive functioning in children,<sup>22,26,43,52,179</sup> and recent studies have reported associations of a number of other environmental contaminants with childhood IQ deficits, including organophosphate pesticides,<sup>69-71</sup> PBDEs,<sup>75</sup> phthalates,<sup>79</sup> and PAHs.<sup>83,180</sup> Exposure to environmental contaminants that reduce IQ has the potential to increase the proportion of the population with IQ less than 70, thus increasing the incidence of intellectual disability in an exposed population.<sup>181-183</sup>

## Indicators in this Section

The four indicators that follow provide the best nationally representative data available on the prevalence of neurodevelopmental disorders among U.S. children over time. The indicators present the number of children ages 5 to 17 years reported to have ever been diagnosed with ADHD (Indicator H6), learning disabilities (Indicator H7), autism (Indicator H8), and intellectual disability (Indicator H9). These four conditions are examples of neurodevelopmental disorders that may be influenced by exposures to environmental contaminants. Intellectual disability and learning disabilities are disorders in which a child’s cognitive or intellectual development is affected, and ADHD is a disorder in which a child’s behavioral development is affected. Autism

spectrum disorders are disorders in which a child's behavior, communication, and social skills are affected. Indicators H6 to H9 have been updated since the publication of the *America's Children and the Environment, Third Edition* (January 2013) to include data through 2017.

**Indicator H6: Percentage of children ages 5 to 17 years reported to have attention-deficit/hyperactivity disorder, by sex, 1997–2017**

**Indicator H7: Percentage of children ages 5 to 17 years reported to have a learning disability, by sex, 1997–2017**

**Indicator H8: Percentage of children ages 5 to 17 years reported to have autism, 1997–2017**

**Indicator H9: Percentage of children ages 5 to 17 years reported to have intellectual disability (mental retardation), 1997–2017**

**About the Indicators:** Indicators H6, H7, H8, and H9 present information about the number of children who are reported to have ever been diagnosed with four different neurodevelopmental disorders: attention-deficit/hyperactivity disorder (ADHD), learning disabilities, autism, and intellectual disability. The data come from a national survey that collects health information from a representative sample of the population each year. The four indicators show how the prevalence of children’s neurodevelopmental disorders has changed over time, and, when possible, how the prevalence differs between boys and girls.

## National Health Interview Survey

The National Health Interview Survey (NHIS) provides nationally representative data on the prevalence of ADHD, learning disabilities, autism, and intellectual disability (mental retardation) in the United States each year. NHIS is a large-scale household interview survey of a representative sample of the civilian noninstitutionalized U.S. population, conducted by the National Center for Health Statistics (NCHS). The interviews are conducted in person at the participants’ homes. From 1997–2005, interviews were conducted for approximately 12,000–14,000 children annually. From 2006–2008, interviews were conducted for approximately 9,000–10,000 children per year. From 2009–2016, interviews were conducted for approximately 11,000–13,000 children per year. In 2017, interviews were conducted for approximately 9,000 children. The data are obtained by asking a parent or other knowledgeable household adult questions regarding the child’s health status. NHIS asks “Has a doctor or health professional ever told you that <child’s name> had Attention Deficit/Hyperactivity Disorder (ADHD) or Attention Deficit Disorder (ADD)? Autism? Mental Retardation?”<sup>i</sup> Another question on the NHIS survey asks “Has a representative from a school or a health professional ever told you that <child’s name> had a learning disability?”

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<sup>i</sup> Starting in 2011, the survey question on mental retardation was revised to ask whether the child had ever been diagnosed with “an intellectual disability, also known as mental retardation.” From 2011 to 2013, the survey question on autism was revised to ask whether the child had ever been diagnosed with “autism/autism spectrum disorder.” Starting in 2014, the survey question on autism was further revised to ask whether the child had ever

## Data Presented in the Indicators

The following indicators display the prevalence of ADHD, learning disabilities, autism, and intellectual disability among U.S. children, for the years 1997–2017. Diagnosing neurodevelopmental disorders in young children can be difficult: many affected children may not receive a diagnosis until they enter preschool or kindergarten. For this reason, the indicators here show children ages 5 to 17 years. Where data are sufficiently reliable, the indicators provide separate prevalence estimates for boys and girls.

Although the NHIS provides national-level data on the prevalence of neurodevelopmental disorders over a span of many years, NHIS data could underestimate the prevalence of neurodevelopmental disorders. Reasons for underestimation may include late identification of affected children and the exclusion of institutionalized children from the NHIS survey population. A diagnosis of a neurodevelopmental disorder depends not only on the presence of particular symptoms and behaviors in a child, but on concerns being raised by a parent or teacher about the child’s behavior, as well as the child’s access to a doctor and the accuracy of the doctor’s diagnosis. Further, the NHIS relies on parents reporting that their child has been diagnosed with a neurodevelopmental disorder, and the accuracy of parental responses could be affected by cultural and other factors.

Long-term trends in these conditions are difficult to detect with certainty due to a lack of data to track prevalence over many years, as well as changes in awareness and diagnostic criteria, which could explain at least part of the observed increasing trends.<sup>184-186</sup> The NHIS questions also do not assess whether a child currently has a disorder; instead, they provide data on whether a child has ever been diagnosed with a disorder, regardless of their current status.

Survey responses for learning disabilities may be more uncertain than for the other three disorders presented. Whereas survey respondents are asked whether the child has been diagnosed with ADHD, autism, or intellectual disability (mental retardation) by a health professional, for learning disabilities an affirmative response may also include a school representative. It is possible that some parents may respond “yes” to the question regarding learning disabilities based on informal comments made at school, rather than a formal evaluation to determine whether the child has any specific learning disability; similarly, they may give a “yes” answer for children with diagnosed disorders that are not learning disabilities. For example, parents of children with intellectual disability might also respond “yes” to the learning disability question, thinking that any learning problems may apply, even though intellectual disability and learning disabilities are distinct conditions.<sup>2</sup>

Up to 2013, autism was the only autism spectrum disorder (ASD) referred to in the survey, and it is not clear how parents of children with other ASDs, i.e., Asperger’s syndrome and PDD-NOS, may have responded. The estimates shown by Indicator H8 for the years 1997 to 2013 could

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been diagnosed with “autism, Asperger’s disorder, pervasive developmental disorder, or autism spectrum disorder.”

represent underestimates of ASD prevalence if parents of children with Asperger's syndrome and PDD-NOS did not answer yes to the NHIS questions about autism.

In addition to the data shown in the indicator graphs, supplemental tables provide information regarding the prevalence of neurodevelopmental disorders for different age groups and prevalence by race/ethnicity, sex, and family income. These comparisons use the most current four years of data available. The data from four years are combined to increase the statistical reliability of the estimates for each race/ethnicity, sex, and family income group. The tables include prevalence estimates for the following race/ethnicity groups: White non-Hispanic, Black non-Hispanic, Asian non-Hispanic, Hispanic, and "All Other Races." The "All Other Races" category includes all other races not specified, together with those individuals who report more than one race. The limits of the sample design and sample size often prevent statistically reliable estimates for smaller race/ethnicity groups. The data are also tabulated for three income groups: all incomes, income below the poverty level, and greater than or equal to the poverty level.

Please see the Introduction to the Health section for discussion of statistical significance testing applied to these indicators.

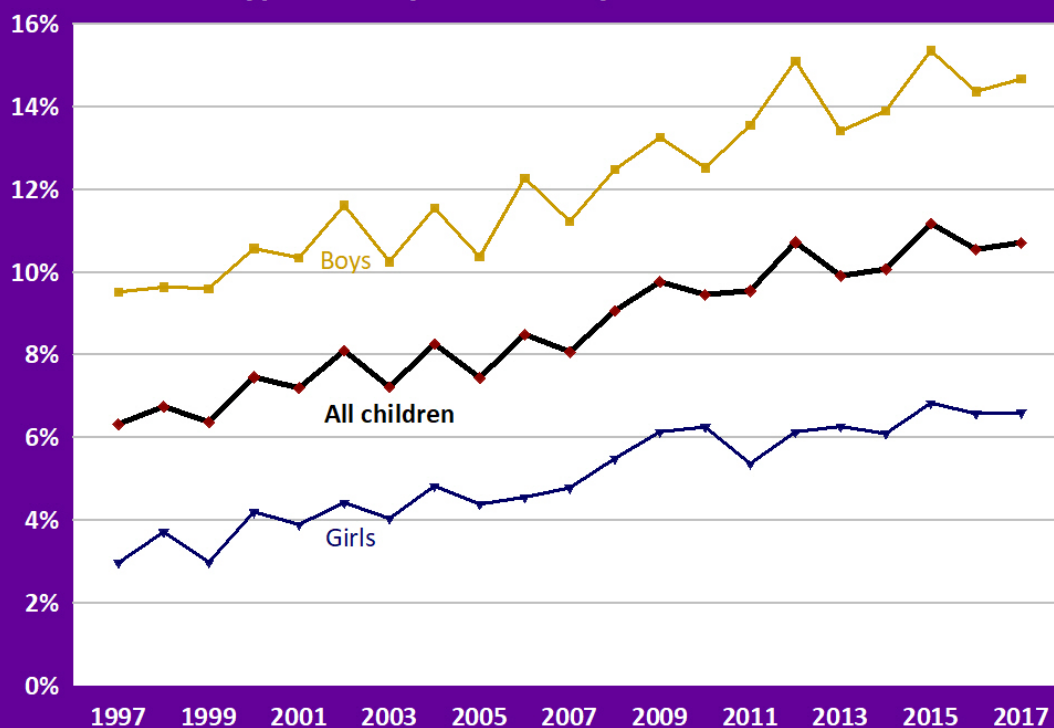
### **Other Estimates of ADHD and Autism Prevalence**

In addition to NHIS, other NCHS studies provide data on prevalence of ADHD and ASDs among children. The National Survey of Children's Health (NSCH), conducted in 2003 by NCHS, found that 7.8% of children ages 4 to 17 years had ever been diagnosed with ADHD. The same survey, when conducted again in 2007, found that 9.5% of children ages 4 to 17 years had ever been diagnosed with ADHD.<sup>7</sup> Both estimates are somewhat higher than the ADHD prevalence estimates from the NHIS for those years. The 2007 NSCH also estimates that 7.2% of children ages 4 to 17 years currently have ADHD. The 2007 NSCH also provides information at the state level: North Carolina had the highest rate, with 15.6% of children ages 4 to 17 years having ever been diagnosed with ADHD; the rate was lowest in Nevada, at 5.6%.<sup>7</sup>

In 2002 and 2006, the Centers for Disease Control and Prevention performed thorough data gathering in selected areas to examine the prevalence of ASDs in eight-year-old children. The ASD prevalence estimate for 2002 was 0.66%, or 1 in 152 eight-year-old children, and the estimate for 2006 was 0.9%, or 1 in 110 eight-year-old children.<sup>8,187</sup> The 2007 NSCH also provides an estimate of 1.1% of children ages 3 to 17 years reported to have ASDs, or about 1 in 90.<sup>188</sup>

## Indicator H6

### Percentage of children ages 5 to 17 years reported to have attention-deficit/hyperactivity disorder, by sex, 1997-2017



Data: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey

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#### [Data Tables for this Topic](#)

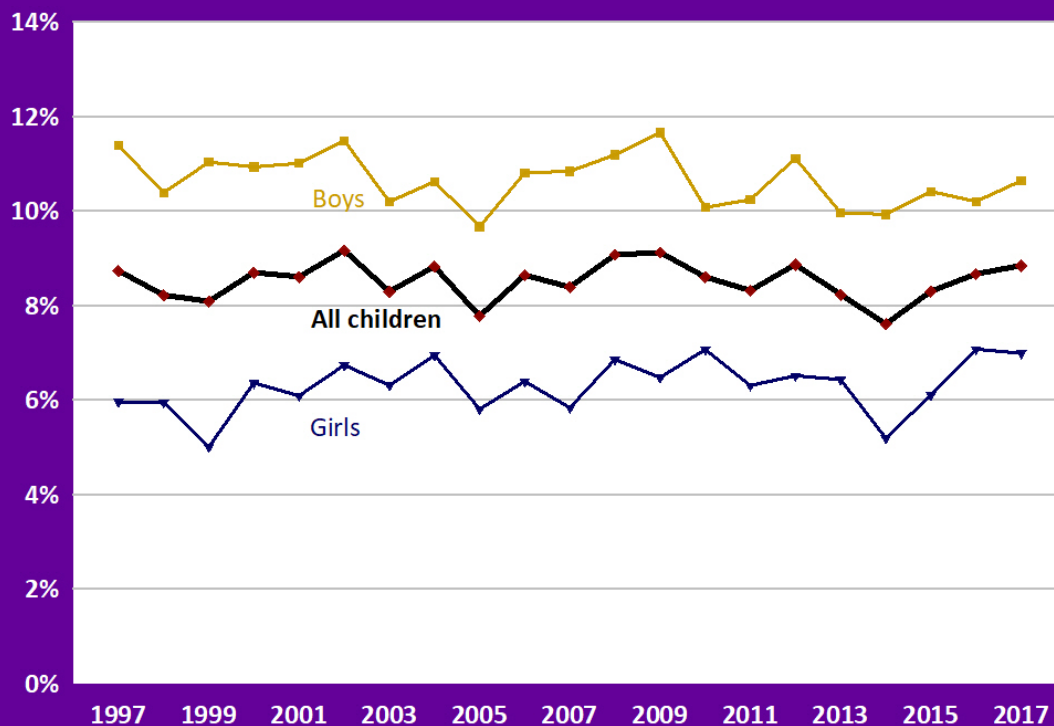
##### Data characterization

- Data for this indicator are obtained from an ongoing annual survey conducted by the National Center for Health Statistics.
- Survey data are representative of the U.S. civilian noninstitutionalized population.
- A parent or other knowledgeable adult in each sampled household is asked questions regarding the child's health status, including if they have ever been told the child has Attention Deficit/Hyperactivity Disorder (ADHD).

- From 1997 to 2017, the proportion of children ages 5 to 17 years reported to have ever been diagnosed with attention-deficit/hyperactivity disorder (ADHD) increased from 6.3% in 1993 to 10.7% in 2017.
  - The increasing trend was statistically significant for children overall, and for both boys and girls considered separately.
- For the years 2014–2017, the percentage of boys reported to have ADHD (14.6%) was higher than the rate for girls (6.5%). This difference was statistically significant. (See Table H6a.)
- In 2014–2017, 13.9% of children of “All Other Races,” 12.6% of White non-Hispanic children, 12.1% of Black non-Hispanic children, 6.7% of Hispanic children, and 2.1% of Asian non-Hispanic children were reported to have ADHD. (See Table H6b.)
  - These differences were statistically significant, with one exception: there was no statistically significant difference between children of “All Other Races” and White non-Hispanic children.
- In 2014–2017, 13.0% of children from families living below the poverty level were reported to have ADHD compared with 10.0% of children from families living at or above the poverty level. This difference was statistically significant. (See Table H6b.)

Indicator H7

### Percentage of children ages 5 to 17 years reported to have a learning disability, by sex, 1997-2017



Data: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey

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#### [Data Tables for this Topic](#)

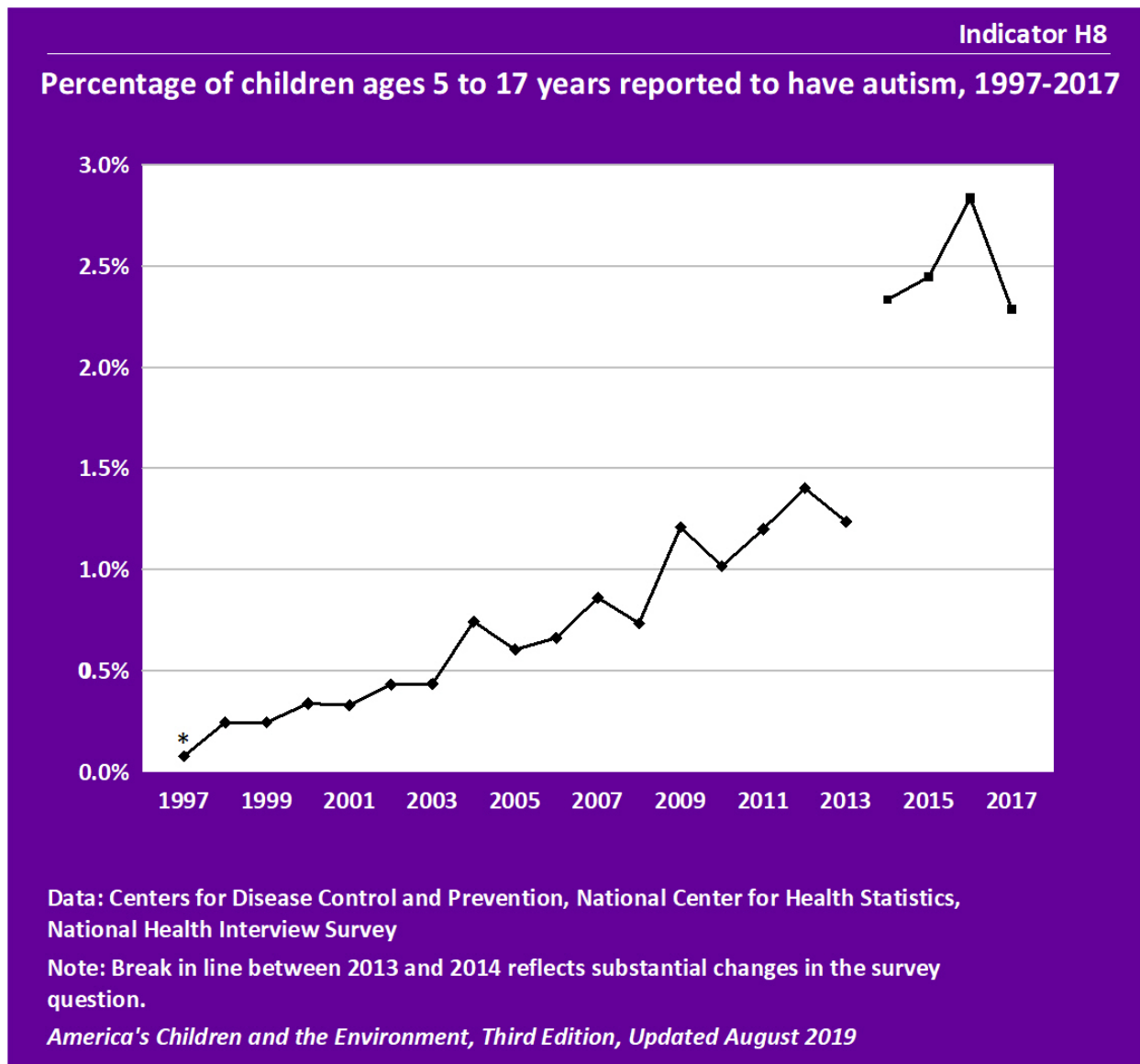
##### Data characterization

- Data for this indicator are obtained from an ongoing annual survey conducted by the National Center for Health Statistics.
- Survey data are representative of the U.S. civilian noninstitutionalized population.
- A parent or other knowledgeable adult in each sampled household is asked questions regarding the child's health status, including if they have ever been told the child has a learning disability.

- In 2017, 8.8% of children ages 5 to 17 years had ever been diagnosed with a learning disability. There was little change in this percentage between 1997 and 2017.



- For the years 2014–2017, the percentage of boys reported to have a learning disability (10.3%) was higher than for girls (6.3%). This difference was statistically significant. (See Table H7a.)
- The reported prevalence of learning disability varies by race and ethnicity. The highest percentages of learning disability are reported for Black non-Hispanic children (10.1%), children of “All Other Races” (9.3%), American Indian or Alaska Native non-Hispanic (8.8%), and White non-Hispanic children (8.6%). By comparison, 7.9% of Hispanic children are reported to have a learning disability, and Asian non-Hispanic children have the lowest prevalence of learning disability, at 2.4%. (See Table H7b.)
  - The prevalence of learning disability reported for Hispanic children and for Asian non-Hispanic children were lower than for the remaining race/ethnicity groups, and these differences were statistically significant. The difference in prevalence between Hispanic and Asian non-Hispanic children was also statistically significant.
- For the years 2014–2017, the percentage of children reported to have a learning disability was higher for children living below the poverty level (12.8%) compared with those living at or above the poverty level (7.3%), a statistically significant difference. (See Table H7b.)



\* The estimate should be interpreted with caution because the standard error of the estimate is relatively large: the relative standard error, RSE, is at least 30% but is less than 40% (RSE = standard error divided by the estimate).

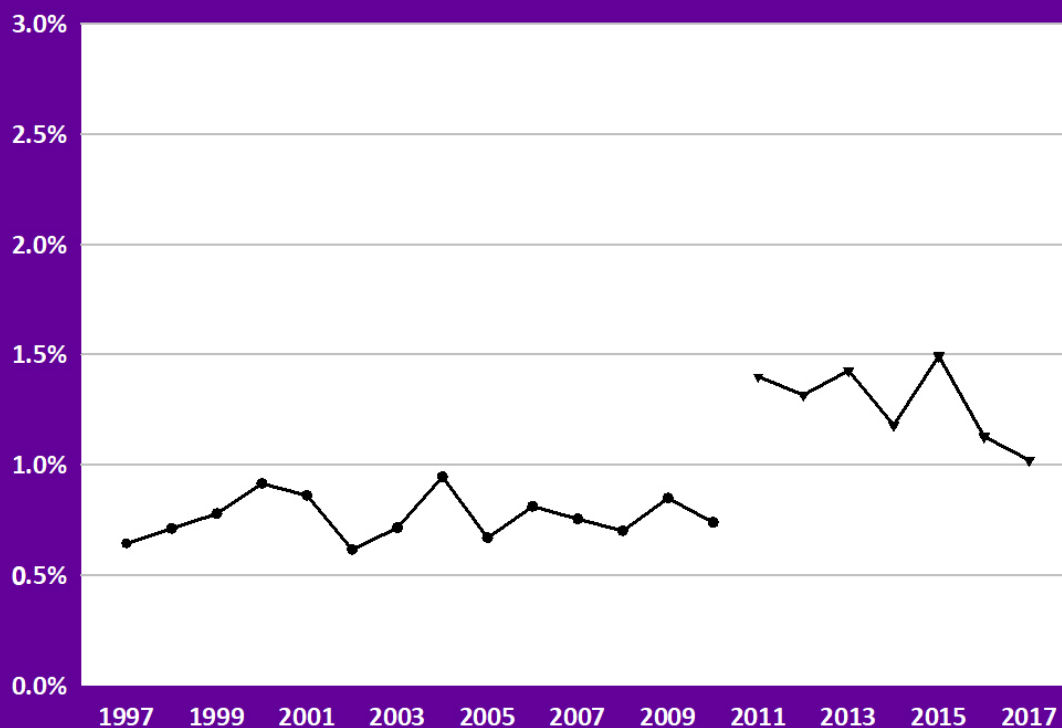
[Data Tables for this Topic](#)

### Data characterization

- Data for this indicator are obtained from an ongoing annual survey conducted by the National Center for Health Statistics.
  - Survey data are representative of the U.S. civilian noninstitutionalized population.
  - A parent or other knowledgeable adult in each sampled household is asked questions regarding the child's health status, including if they have ever been told the child has autism. From 2011 to 2013, the term “autism” in the question was revised to “autism/autism spectrum disorder.” Starting in 2014, the term “autism” in the question was revised to “autism, Asperger's disorder, pervasive developmental disorder, or autism spectrum disorder.”
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- The percentage of children ages 5 to 17 years reported to have ever been diagnosed with autism rose from 0.1% in 1997 to 1.2% in 2013. This increasing trend was statistically significant.
    - Between 2014 and 2017, the rates of reported autism ranged from 2.3% to 2.8%. The higher reported percentages in these years compared with prior years might be due in part to the recent broadening of the definition of autism used in the survey question, as noted in the above “Data characterization” box.
  - For the years 2014–2017, the rate of reported autism was about four times higher in boys than in girls, 3.8% and 1.1%, respectively. This difference was statistically significant. (See Table H8a.)
  - The reported prevalence of autism varies by race/ethnicity. The highest prevalence of autism is for children of “All Other Races” (3.0%) and White non-Hispanic children (2.9%). Autism prevalence was lower among Black non-Hispanic children (2.2%), Hispanic children (1.8%), and Asian non-Hispanic children (1.6%). (See Table H8b.)
    - The prevalence of autism for both White non-Hispanic children and children of “All Other Races” was statistically significantly different from the prevalence for both Asian non-Hispanic children and Hispanic children.
  - For the years 2014–2017, the prevalence of autism was similar for children living below the poverty level and those living at or above the poverty level. (See Table H8b.)

## Indicator H9

### Percentage of children ages 5 to 17 years reported to have intellectual disability (mental retardation), 1997-2017



Data: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey

Note: Break in line between 2010 and 2011 reflects substantial changes in the survey question.

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#### [Data Tables for this Topic](#)

##### Data characterization

- Data for this indicator are obtained from an ongoing annual survey conducted by the National Center for Health Statistics.
- Survey data are representative of the U.S. civilian noninstitutionalized population.
- A parent or other knowledgeable adult in each sampled household is asked questions regarding the child's health status, including if they have ever been told the child has mental retardation.
- A parent or other knowledgeable adult in each sampled household is asked questions regarding the child's health status, including if they have ever been told the child has mental retardation. Starting in 2011, the term "mental retardation" in the question was revised to "an intellectual disability, otherwise known as mental retardation."

- In 2017, 1.0% of children ages 5 to 17 years were reported to have ever been diagnosed with intellectual disability (mental retardation). This percentage fluctuated between 0.6% and 0.9% from 1997 to 2010, and was between 1.0% and 1.5% from 2011 to 2017.
  - The higher reported percentages in 2011 to 2017 compared with prior years might be in part due to the revision of the survey question wording, as noted in the above “Data characterization” box.
- In 2014–2017, the percentage of boys reported to have intellectual disability (1.5%) was higher than for girls (0.9%). This difference was statistically significant. (See Table H9a.)
- In 2014–2017, the reported prevalence of intellectual disability was lowest for Asian non-Hispanic children (0.5%) and was between 1.2% and 1.4% for the other race/ethnicity groups. The differences between Asian non-Hispanic children and children of other race/ethnicity groups were statistically significant. (See Table H9b.)
- In 2014–2017, 2.0% of children from families with incomes below the poverty level were reported to have intellectual disability, compared with 1.0% of children from families at or above the poverty level, a statistically significant difference. (See Table H9b.)

## References

1. Boyle, C.A., S. Boulet, L.A. Schieve, R.A. Cohen, S.J. Blumberg, M. Yeargin-Allsopp, S. Visser, and M.D. Kogan. 2011. Trends in the prevalence of developmental disabilities in US Children, 1997–2008. *Pediatrics* 127 (6):1034-42.
2. Pastor, P.N., and C.A. Reuben. 2008. Diagnosed attention deficit hyperactivity disorder and learning disability: United States, 2004-2006. *Vital and Health Statistics* 10 (237).
3. Grandjean, P., and P.J. Landrigan. 2006. Developmental neurotoxicity of industrial chemicals. *Lancet* 368 (9553):2167-78.
4. Newschaffer, C.J., M.D. Falb, and J.G. Gurney. 2005. National autism prevalence trends from United States special education data. *Pediatrics* 115 (3):e277-82.
5. Prior, M. 2003. Is there an increase in the prevalence of autism spectrum disorders? *Journal of Paediatrics and Child Health* 39 (2):81-2.
6. Rutter, M. 2005. Incidence of autism spectrum disorders: changes over time and their meaning. *Acta Paediatrica* 94 (1):2-15.
7. Centers for Disease Control and Prevention. 2010. Increasing prevalence of parent-reported attention-deficit/hyperactivity disorder among children --- United States, 2003 and 2007. *Morbidity and Mortality Weekly Report* 59 (44):1439-43.
8. Centers for Disease Control and Prevention. 2009. Prevalence of autism spectrum disorders --- autism and developmental disabilities monitoring network, United States, 2006. *Morbidity and Mortality Weekly Report* 58 (SS 10):1-20.
9. Hertz-Picciotto, I., and L. Delwiche. 2009. The rise in autism and the role of age at diagnosis. *Epidemiology* 20 (1):84-90.
10. Newschaffer, C.J. 2006. Investigating diagnostic substitution and autism prevalence trends. *Pediatrics* 117 (4):1436-7.
11. Grupp-Phelan, J., J.S. Harman, and K.J. Kelleher. 2007. Trends in mental health and chronic condition visits by children presenting for care at U.S. emergency departments. *Public Health Reports* 122 (1):55-61.
12. Kelleher, K.J., T.K. McNerny, W.P. Gardner, G.E. Childs, and R.C. Wasserman. 2000. Increasing identification of psychosocial problems: 1979-1996. *Pediatrics* 105 (6):1313-21.
13. U.S. Department of Education. 2007. *27th Annual (2005) Report to Congress on the Implementation of the Individuals with Disabilities Education Act, Vol. 1*. Washington, DC.
14. Aarnoudse-Moens, C.S.H., N. Weisglas-Kuperus, J.B. van Goudoever, and J. Oosterlaan. 2009. Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children. *Pediatrics* 124 (2):717-728.
15. Banerjee, T.D., F. Middleton, and S.V. Faraone. 2007. Environmental risk factors for attention-deficit hyperactivity disorder. *Acta Paediatrica* 96 (9):1269-1274.
16. Bhutta, A.T., M.A. Cleves, P.H. Casey, M.M. Craddock, and K.J.S. Anand. 2002. Cognitive and behavioral outcomes of school-aged children who were born preterm. *JAMA: The Journal of the American Medical Association* 288 (6):728-737.
17. Herrmann, M., K. King, and M. Weitzman. 2008. Prenatal tobacco smoke and postnatal secondhand smoke exposure and child neurodevelopment. *Current Opinion in Pediatrics* 20 (2):184-190.
18. Institute of Medicine. 2007. *Preterm Birth: Causes, Consequences, and Prevention*. Edited by R. E. Behrman and A. S. Butler. Washington, DC: The National Academies Press.
19. Linnet, K.M., S. Dalsgaard, C. Obel, K. Wisborg, T.B. Henriksen, A. Rodriguez, A. Kotimaa, I. Moilanen, P.H. Thomsen, J. Olsen, et al. 2003. Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity

- disorder and associated behaviors: review of the current evidence. *The American Journal of Psychiatry* 160 (6):1028-40.
20. Nigg, J.T. 2006. *What Causes ADHD? Understanding What Goes Wrong and Why*. New York: The Guilford Press.
21. Weiss, B., and D.C. Bellinger. 2006. Social ecology of children's vulnerability to environmental pollutants. *Environmental Health Perspectives* 114 (10):1479-1485.
22. National Toxicology Program. 2012. *NTP Monograph on Health Effects of Low-Level Lead*. Research Triangle Park, NC: National Institute of Environmental Health Sciences, National Toxicology Program. <http://ntp.niehs.nih.gov/go/36443>.
23. U.S. Environmental Protection Agency. 1997. *Mercury Study Report to Congress Volumes I to VII*. Washington DC: U.S. Environmental Protection Agency Office of Air Quality Planning and Standards and Office of Research and Development. EPA-452/R-97-003. <http://www.epa.gov/hg/report.htm>.
24. Amin-Zaki, L., S. Elhassani, M.A. Majeed, T.W. Clarkson, R.A. Doherty, and M. Greenwood. 1974. Intra-uterine methylmercury poisoning in Iraq. *Pediatrics* 54 (5):587-95.
25. Harada, M. 1995. Minamata disease: methylmercury poisoning in Japan caused by environmental pollution. *Critical Reviews in Toxicology* 25 (1):1-24.
26. National Research Council. 2000. *Toxicological Effects of Methylmercury*. Washington, DC: National Academy Press.
27. Budtz-Jorgensen, E., P. Grandjean, and P. Weihe. 2007. Separation of risks and benefits of seafood intake. *Environmental Health Perspectives* 115 (3):323-7.
28. Crump, K.S., T. Kjellstrom, A.M. Shipp, A. Silvers, and A. Stewart. 1998. Influence of prenatal mercury exposure upon scholastic and psychological test performance: benchmark analysis of a New Zealand cohort. *Risk Analysis* 18 (6):701-13.
29. Debes, F., E. Budtz-Jorgensen, P. Weihe, R.F. White, and P. Grandjean. 2006. Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years. *Neurotoxicology and Teratology* 28 (5):536-47.
30. Grandjean, P., P. Weihe, R.F. White, F. Debes, S. Araki, K. Yokoyama, K. Murata, N. Sorensen, R. Dahl, and P.J. Jorgensen. 1997. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicology and Teratology* 19 (6):417-28.
31. Kjellstrom, T., P. Kennedy, S. Wallis, and C. Mantell. 1986. *Physical and mental development of children with prenatal exposure to mercury from fish. Stage 1: Preliminary tests at age 4*. Sweden: Swedish National Environmental Protection Board.
32. Oken, E., and D.C. Bellinger. 2008. Fish consumption, methylmercury and child neurodevelopment. *Current Opinion in Pediatrics* 20 (2):178-83.
33. Myers, G.J., P.W. Davidson, C. Cox, C.F. Shamlaye, D. Palumbo, E. Cernichiari, J. Sloane-Reeves, G.E. Wilding, J. Kost, L.S. Huang, et al. 2003. Prenatal methylmercury exposure from ocean fish consumption in the Seychelles child development study. *Lancet* 361 (9370):1686-92.
34. Davidson, P.W., J.J. Strain, G.J. Myers, S.W. Thurston, M.P. Bonham, C.F. Shamlaye, A. Stokes-Riner, J.M. Wallace, P.J. Robson, E.M. Duffy, et al. 2008. Neurodevelopmental effects of maternal nutritional status and exposure to methylmercury from eating fish during pregnancy. *Neurotoxicology* 29 (5):767-75.
35. Lynch, M.L., L.S. Huang, C. Cox, J.J. Strain, G.J. Myers, M.P. Bonham, C.F. Shamlaye, A. Stokes-Riner, J.M. Wallace, E.M. Duffy, et al. 2011. Varying coefficient function models to explore interactions between maternal nutritional status and prenatal methylmercury toxicity in the Seychelles Child Development Nutrition Study. *Environmental Research* 111 (1):75-80.

36. Strain, J.J., P.W. Davidson, M.P. Bonham, E.M. Duffy, A. Stokes-Riner, S.W. Thurston, J.M. Wallace, P.J. Robson, C.F. Shamlaye, L.A. Georger, et al. 2008. Associations of maternal long-chain polyunsaturated fatty acids, methyl mercury, and infant development in the Seychelles Child Development Nutrition Study. *Neurotoxicology* 29 (5):776-782.
37. Lederman, S.A., R.L. Jones, K.L. Caldwell, V. Rauh, S.E. Sheets, D. Tang, S. Viswanathan, M. Becker, J.L. Stein, R.Y. Wang, et al. 2008. Relation between cord blood mercury levels and early child development in a World Trade Center cohort. *Environmental Health Perspectives* 116 (8):1085-91.
38. Oken, E., J.S. Radesky, R.O. Wright, D.C. Bellinger, C.J. Amarasiriwardena, K.P. Kleinman, H. Hu, and M.W. Gillman. 2008. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort. *American Journal of Epidemiology* 167 (10):1171-81.
39. Jacobson, J.L., and S.W. Jacobson. 2003. Prenatal exposure to polychlorinated biphenyls and attention at school age. *Journal of Pediatrics* 143 (6):780-8.
40. Sagiv, S.K., S.W. Thurston, D.C. Bellinger, P.E. Tolbert, L.M. Altshul, and S.A. Korrick. 2010. Prenatal organochlorine exposure and behaviors associated with attention deficit hyperactivity disorder in school-aged children. *American Journal of Epidemiology* 171 (5):593-601.
41. Stewart, P., S. Fitzgerald, J. Reihman, B. Gump, E. Lonky, T. Darvill, J. Pagano, and P. Hauser. 2003. Prenatal PCB exposure, the corpus callosum, and response inhibition. *Environmental Health Perspectives* 111 (13):1670-7.
42. Stewart, P., J. Reihman, B. Gump, E. Lonky, T. Darvill, and J. Pagano. 2005. Response inhibition at 8 and 9 1/2 years of age in children prenatally exposed to PCBs. *Neurotoxicology and Teratology* 27 (6):771-80.
43. Stewart, P.W., E. Lonky, J. Reihman, J. Pagano, B.B. Gump, and T. Darvill. 2008. The relationship between prenatal PCB exposure and intelligence (IQ) in 9-year-old children. *Environmental Health Perspectives* 116 (10):1416-22.
44. Stewart, P.W., D.M. Sargent, J. Reihman, B.B. Gump, E. Lonky, T. Darvill, H. Hicks, and J. Pagano. 2006. Response inhibition during Differential Reinforcement of Low Rates (DRL) schedules may be sensitive to low-level polychlorinated biphenyl, methylmercury, and lead exposure in children. *Environmental Health Perspectives* 114 (12):1923-9.
45. Vreugdenhil, H.J., P.G. Mulder, H.H. Emmen, and N. Weisglas-Kuperus. 2004. Effects of perinatal exposure to PCBs on neuropsychological functions in the Rotterdam cohort at 9 years of age. *Neuropsychology* 18 (1):185-93.
46. Darvill, T., E. Lonky, J. Reihman, P. Stewart, and J. Pagano. 2000. Prenatal exposure to PCBs and infant performance on the Fagan test of infant intelligence. *Neurotoxicology* 21 (6):1029-38.
47. Jacobson, J.L., and S.W. Jacobson. 1996. Intellectual impairment in children exposed to polychlorinated biphenyls in utero. *New England Journal of Medicine* 335 (11):783-9.
48. Jacobson, J.L., and S.W. Jacobson. 1997. Teratogen update: polychlorinated biphenyls. *Teratology* 55 (5):338-347.
49. Patandin, S., C.I. Lanting, P.G. Mulder, E.R. Boersma, P.J. Sauer, and N. Weisglas-Kuperus. 1999. Effects of environmental exposure to polychlorinated biphenyls and dioxins on cognitive abilities in Dutch children at 42 months of age. *Journal of Pediatrics* 134 (1):33-41.
50. Stewart, P., J. Reihman, E. Lonky, T. Darvill, and J. Pagano. 2000. Prenatal PCB exposure and neonatal behavioral assessment scale (NBAS) performance. *Neurotoxicology and Teratology* 22 (1):21-9.
51. Walkowiak, J., J.A. Wiener, A. Fastabend, B. Heinzow, U. Kramer, E. Schmidt, H.J. Steingruber, S. Wundram, and G. Winneke. 2001. Environmental exposure to polychlorinated biphenyls and quality of the home environment: effects on psychodevelopment in early childhood. *Lancet* 358 (9293):1602-7.
52. Schantz, S.L., J.J. Widholm, and D.C. Rice. 2003. Effects of PCB exposure on neuropsychological function in children. *Environmental Health Perspectives* 111 (3):357-576.



53. Jacobson, J.L., S.W. Jacobson, and H.E. Humphrey. 1990. Effects of exposure to PCBs and related compounds on growth and activity in children. *Neurotoxicology and Teratology* 12 (4):319-26.
54. Boucher, O., G. Muckle, and C.H. Bastien. 2009. Prenatal exposure to polychlorinated biphenyls: a neuropsychologic analysis. *Environmental Health Perspectives* 117 (1):7-16.
55. Eubig, P.A., A. Aguiar, and S.L. Schantz. 2010. Lead and PCBs as risk factors for attention deficit/hyperactivity disorder. *Environmental Health Perspectives* 118 (12):1654-1667.
56. Ribas-Fito, N., M. Sala, M. Kogevinas, and J. Sunyer. 2001. Polychlorinated biphenyls (PCBs) and neurological development in children: a systematic review. *Journal of Epidemiology and Community Health* 55 (8):537-46.
57. Schantz, S.L., J.C. Gardiner, D.M. Gasior, R.J. McCaffrey, A.M. Sweeney, and H.E.B. Humphrey. 2004. Much Ado About Something: The Weight of Evidence for PCB Effects on Neuropsychological Function. *Psychology in the Schools* 41 (6):669-679.
58. Wigle, D.T., T.E. Arbuckle, M.C. Turner, A. Berube, Q. Yang, S. Liu, and D. Krewski. 2008. Epidemiologic evidence of relationships between reproductive and child health outcomes and environmental chemical contaminants. *Journal of Toxicology and Environmental Health Part B Critical Reviews* 11 (5-6):373-517.
59. Agency for Toxic Substances and Disease Registry (ATSDR). 2000. *Toxicological Profile for Polychlorinated Biphenyls (PCBs)*. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=142&tid=26>.
60. Chen, Y.C., Y.L. Guo, C.C. Hsu, and W.J. Rogan. 1992. Cognitive development of Yu-Cheng ("oil disease") children prenatally exposed to heat-degraded PCBs. *Journal of the American Medical Association* 268 (22):3213-8.
61. Chen, Y.C., M.L. Yu, W.J. Rogan, B.C. Gladen, and C.C. Hsu. 1994. A 6-year follow-up of behavior and activity disorders in the Taiwan Yu-cheng children. *American Journal of Public Health* 84 (3):415-21.
62. Lai, T.J., X. Liu, Y.L. Guo, N.W. Guo, M.L. Yu, C.C. Hsu, and W.J. Rogan. 2002. A cohort study of behavioral problems and intelligence in children with high prenatal polychlorinated biphenyl exposure. *Archives of General Psychiatry* 59 (11):1061-6.
63. Rogan, W.J., B.C. Gladen, K.L. Hung, S.L. Koong, L.Y. Shih, J.S. Taylor, Y.C. Wu, D. Yang, N.B. Ragan, and C.C. Hsu. 1988. Congenital poisoning by polychlorinated biphenyls and their contaminants in Taiwan. *Science* 241 (4863):334-6.
64. Centers for Disease Control and Prevention. 2009. *Fourth National Report on Human Exposure to Environmental Chemicals*. Atlanta, GA: CDC. <http://www.cdc.gov/exposurereport/>.
65. Eskenazi, B., A. Bradman, and R. Castorina. 1999. Exposures of children to organophosphate pesticides and their potential adverse health effects. *Environmental Health Perspectives* 107 (Suppl. 3):409-19.
66. Huen, K., Harley, K., Brooks, J., Hubbard, A., Bradman, A., Eskenazi, B., Holland, N. 2009. Developmental changes in PON1 enzyme activity in young children and effects of PON1 polymorphisms. *Environmental Health Perspectives* 117 (10):1632-8.
67. Marks, A.R., K. Harley, A. Bradman, K. Kogut, D.B. Barr, C. Johnson, N. Calderon, and B. Eskenazi. 2010. Organophosphate pesticide exposure and attention in young Mexican-American children: the CHAMACOS study. *Environmental Health Perspectives* 118 (12):1768-74.
68. Bouchard, M.F., D.C. Bellinger, R.O. Wright, and M.G. Weisskopf. 2010. Attention-Deficit/Hyperactivity Disorder and urinary metabolites of organophosphate pesticides. *Pediatrics* 125 (6):e1270-e1277.
69. Bouchard, M.F., J. Chevrier, K.G. Harley, K. Kogut, M. Vedar, N. Calderon, C. Trujillo, C. Johnson, A. Bradman, D.B. Barr, et al. 2011. Prenatal exposure to organophosphate pesticides and IQ in 7-year old children. *Environmental Health Perspectives* doi: 10.1289/ehp.1003185.

70. Engel, S.M., J. Wetmur, J. Chen, C. Zhu, D.B. Barr, R.L. Canfield, and M.S. Wolff. 2011. Prenatal exposure to organophosphates, paraoxonase 1, and cognitive development in childhood. *Environmental Health Perspectives* doi: 10.1289/ehp.1003183.
71. Rauh, V., S. Arunajadai, M. Horton, F. Perera, L. Hoepner, D.B. Barr, and R. Whyatt. 2011. 7-Year neurodevelopmental scores and prenatal exposure to chlorpyrifos, a common agricultural pesticide. *Environmental Health Perspectives* doi: 10.1289/ehp.1003160.
72. Costa, L.G., G. Giordano, S. Tagliaferri, A. Caglieri, and A. Mutti. 2008. Polybrominated diphenyl ether (PBDE) flame retardants: environmental contamination, human body burden and potential adverse health effects. *Acta Biomed* 79 (3):172-83.
73. Gee, J.R., and V.C. Moser. 2008. Acute postnatal exposure to brominated diphenylether 47 delays neuromotor ontogeny and alters motor activity in mice. *Neurotoxicology and Teratology* 30 (2):79-87.
74. Rice, D.C., E.A. Reeve, A. Herlihy, R.T. Zoeller, W.D. Thompson, and V.P. Markowski. 2007. Developmental delays and locomotor activity in the C57BL6/J mouse following neonatal exposure to the fully-brominated PBDE, decabromodiphenyl ether. *Neurotoxicology and Teratology* 29 (4):511-20.
75. Herbstman, J.B., A. Sjodin, M. Kurzon, S.A. Lederman, R.S. Jones, V. Rauh, L.L. Needham, D. Tang, M. Niedzwiecki, R.Y. Wang, et al. 2010. Prenatal exposure to PBDEs and neurodevelopment. *Environmental Health Perspectives* 118 (5):712-9.
76. Roze, E., L. Meijer, A. Bakker, K.N. Van Braeckel, P.J. Sauer, and A.F. Bos. 2009. Prenatal exposure to organohalogens, including brominated flame retardants, influences motor, cognitive, and behavioral performance at school age. *Environmental Health Perspectives* 117 (12):1953-8.
77. Engel, S.M., A. Miodovnik, R.L. Canfield, C. Zhu, M.J. Silva, A.M. Calafat, and M.S. Wolff. 2010. Prenatal phthalate exposure is associated with childhood behavior and executive functioning. *Environmental Health Perspectives* 118 (4):565-71.
78. Miodovnik, A., S.M. Engel, C. Zhu, X. Ye, L.V. Soorya, M.J. Silva, A.M. Calafat, and M.S. Wolff. 2011. Endocrine disruptors and childhood social impairment. *Neurotoxicology* 32 (2):261-267.
79. Cho, S.-C., S.-Y. Bhang, Y.-C. Hong, M.-S. Shin, B.-N. Kim, J.-W. Kim, H.-J. Yoo, I.H. Cho, and H.-W. Kim. 2010. Relationship between environmental phthalate exposure and the intelligence of school-age children. *Environmental Health Perspectives* 118 (7):1027-1032.
80. Kim, B.N., S.C. Cho, Y. Kim, M.S. Shin, H.J. Yoo, J.W. Kim, Y.H. Yang, H.W. Kim, S.Y. Bhang, and Y.C. Hong. 2009. Phthalates exposure and attention-deficit/hyperactivity disorder in school-age children. *Biological Psychiatry* 66 (10):958-63.
81. National Toxicology Program. 2008. *NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Bisphenol A*. Research Triangle Park, NC: National Institute of Environmental Health Sciences, National Toxicology Program. <http://ntp.niehs.nih.gov/ntp/ohat/bisphenol/bisphenol.pdf>.
82. Braun, J.M., K. Yolton, K.N. Dietrich, R. Hornung, X. Ye, A.M. Calafat, and B.P. Lanphear. 2009. Prenatal bisphenol A exposure and early childhood behavior. *Environmental Health Perspectives* 117 (12):1945-1952.
83. Perera, F.P., Z. Li, R. Whyatt, L. Hoepner, S. Wang, D. Camann, and V. Rauh. 2009. Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years. *Pediatrics* 124 (2):e195-202.
84. Perera, F.P., S. Wang, J. Vishnevetsky, B. Zhang, K.J. Cole, D. Tang, V. Rauh, and D.H. Phillips. 2011. PAH/Aromatic DNA Adducts in Cord Blood and Behavior Scores in New York City Children. *Environmental Health Perspectives* doi:10.1289/ehp.1002705.
85. Smith, A.H., and C.M. Steinmaus. 2009. Health effects of arsenic and chromium in drinking water: recent human findings. *Annual Review of Public Health* 30:107-22.
86. Sambu, S., and R. Wilson. 2008. Arsenic in food and water--a brief history. *Toxicology and Industrial Health* 24 (4):217-26.

87. U.S. Environmental Protection Agency. 2011. *Perchlorate* Retrieved February 11, 2011 from <http://www.epa.gov/safewater/contaminants/unregulated/perchlorate.html>.
88. Kirk, A.B., P.K. Martinelango, K. Tian, A. Dutta, E.E. Smith, and P.K. Dasgupta. 2005. Perchlorate and iodide in dairy and breast milk. *Environmental Science & Technology* 39 (7):2011-7.
89. Sanchez, C.A., L.M. Barraj, B.C. Blount, C.G. Scrafford, L. Valentin-Blasini, K.M. Smith, and R.I. Krieger. 2009. Perchlorate exposure from food crops produced in the lower Colorado River region. *Journal of Exposure Science & Environmental Epidemiology* 19 (4):359-68.
90. Greer, M.A., G. Goodman, R.C. Pleus, and S.E. Greer. 2002. Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. *Environmental Health Perspectives* 110 (9):927-37.
91. National Research Council. 2005. *Health Implications of Perchlorate Ingestion*. Washington, DC: National Academies Press. [http://www.nap.edu/catalog.php?record\\_id=11202](http://www.nap.edu/catalog.php?record_id=11202).
92. Haddow, J.E., G.E. Palomaki, W.C. Allan, J.R. Williams, G.J. Knight, J. Gagnon, C.E. O'Heir, M.L. Mitchell, R.J. Hermos, S.E. Waisbren, et al. 1999. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *New England Journal of Medicine* 341 (8):549-55.
93. Miller, M.D., K.M. Crofton, D.C. Rice, and R.T. Zoeller. 2009. Thyroid-disrupting chemicals: interpreting upstream biomarkers of adverse outcomes. *Environmental Health Perspectives* 117 (7):1033-41.
94. Morreale de Escobar, G., M.J. Obregon, and F. Escobar del Rey. 2000. Is neuropsychological development related to maternal hypothyroidism or to maternal hypothyroxinemia? *The Journal of Clinical Endocrinology and Metabolism* 85 (11):3975-87.
95. Bellinger, D.C. 2008. Lead neurotoxicity and socioeconomic status: conceptual and analytical issues. *Neurotoxicology* 29 (5):828-32.
96. Rice, D.C. 2000. Parallels between attention deficit hyperactivity disorder and behavioral deficits produced by neurotoxic exposure in monkeys. *Environmental Health Perspectives* 108 (Suppl. 3):405-408.
97. Rodier, P.M. 1995. Developing brain as a target of toxicity. *Environmental Health Perspectives* 103 Suppl. 6:73-6.
98. American Psychiatric Association. 2000. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision*. Washington D.C.: American Psychiatric Association.
99. American Psychiatric Association. 1987. *Diagnostic and Statistical Manual of Mental Disorders, Third Edition Text Revision (DSM-III-R)*. Washington, D.C.
100. Larson, K., S.A. Russ, R.S. Kahn, and N. Halfon. 2011. Patterns of comorbidity, functioning, and service use for U.S. children with ADHD, 2007. *Pediatrics* 127 (3):462-470.
101. Aguiar, A., P.A. Eubig, and S.L. Schantz. 2010. Attention deficit/hyperactivity disorder: a focused overview for children's environmental health researchers. *Environmental Health Perspectives* 118 (12):1646-53.
102. Barkley, R.A. 2006. *Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment, Third Edition*. New York: The Guilford Press.
103. Biederman, J., and S.V. Faraone. 2005. Attention-deficit hyperactivity disorder. *Lancet* 366 (9481):237-48.
104. Faraone, S.V., and E. Mick. 2010. Molecular genetics of attention deficit hyperactivity disorder. *Psychiatric Clinics of North America* 33 (1):159-80.
105. Kieling, C., R.R. Goncalves, R. Tannock, and F.X. Castellanos. 2008. Neurobiology of attention deficit hyperactivity disorder. *Child and Adolescent Psychiatric Clinics of North America* 17 (2):285-307, viii.
106. Thapar, A., K. Langley, P. Asherson, and M. Gill. 2007. Gene-environment interplay in attention-deficit hyperactivity disorder and the importance of a developmental perspective. *The British Journal of Psychiatry* 190:1-3.

107. Langley, K., F. Rice, M.B. van den Bree, and A. Thapar. 2005. Maternal smoking during pregnancy as an environmental risk factor for attention deficit hyperactivity disorder behaviour. A review. *Minerva Pediatrica* 57 (6):359-71.
108. Nigg, J., M. Nikolas, and S.A. Burt. 2010. Measured gene-by-environment interaction in relation to attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry* 49 (9):863-73.
109. Braun, J.M., R.S. Kahn, T. Froehlich, P. Auinger, and B.P. Lanphear. 2006. Exposures to environmental toxicants and attention deficit hyperactivity disorder in U.S. children. *Environmental Health Perspectives* 114 (12):1904-9.
110. Froehlich, T.E., B.P. Lanphear, P. Auinger, R. Hornung, J.N. Epstein, J. Braun, and R.S. Kahn. 2009. Association of tobacco and lead exposures with attention-deficit/hyperactivity disorder. *Pediatrics* 124 (6):e1054-63.
111. Ha, M., H.J. Kwon, M.H. Lim, Y.K. Jee, Y.C. Hong, J.H. Leem, J. Sakong, J.M. Bae, S.J. Hong, Y.M. Roh, et al. 2009. Low blood levels of lead and mercury and symptoms of attention deficit hyperactivity in children: a report of the children's health and environment research (CHEER). *Neurotoxicology* 30 (1):31-6.
112. Nigg, J.T., G.M. Knottnerus, M.M. Martel, M. Nikolas, K. Cavanagh, W. Karmaus, and M.D. Rappley. 2008. Low blood lead levels associated with clinically diagnosed attention-deficit/hyperactivity disorder and mediated by weak cognitive control. *Biological Psychiatry* 63 (3):325-31.
113. Nigg, J.T., M. Nikolas, G. Mark Knottnerus, K. Cavanagh, and K. Friderici. 2010. Confirmation and extension of association of blood lead with attention-deficit/hyperactivity disorder (ADHD) and ADHD symptom domains at population-typical exposure levels. *The Journal of Child Psychology and Psychiatry* 51 (1):58-65.
114. Roy, A., D. Bellinger, H. Hu, J. Schwartz, A.S. Ettinger, R.O. Wright, M. Bouchard, K. Palaniappan, and K. Balakrishnan. 2009. Lead exposure and behavior among young children in Chennai, India. *Environmental Health Perspectives* 117 (10):1607-11.
115. Wang, H.-L., X.-T. Chen, B. Yang, F.-L. Ma, S. Wang, M.-L. Tang, N.-G. Hao, and D.-Y. Ruan. 2008. Case-control study of blood lead levels and attention-deficit hyperactivity disorder in Chinese children. *Environmental Health Perspectives* 116 (10):1401-1406.
116. Canfield, R.L., M.H. Gendle, and D.A. Cory-Slechta. 2004. Impaired neuropsychological functioning in lead-exposed children. *Developmental Neuropsychology* 26 (1):513-40.
117. Chiodo, L.M., S.W. Jacobson, and J.L. Jacobson. 2004. Neurodevelopmental effects of postnatal lead exposure at very low levels. *Neurotoxicology and Teratology* 26 (3):359-71.
118. Nicolescu, R., C. Petcu, A. Cordeanu, K. Fabritius, M. Schlumpf, R. Krebs, U. Kramer, and G. Winneke. 2010. Environmental exposure to lead, but not other neurotoxic metals, relates to core elements of ADHD in Romanian children: performance and questionnaire data. *Environmental Research* 110 (5):476-83.
119. Surkan, P.J., A. Zhang, F. Trachtenberg, D.B. Daniel, S. McKinlay, and D.C. Bellinger. 2007. Neuropsychological function in children with blood lead levels <10 microg/dL. *Neurotoxicology* 28 (6):1170-7.
120. Rice, D.C. 1996. Behavioral effects of lead: commonalities between experimental and epidemiologic data. *Environmental Health Perspectives* 104 (Suppl. 2):337-51.
121. Rossi-George, A., M.B. Virgolini, D. Weston, M. Thiruchelvam, and D.A. Cory-Slechta. 2011. Interactions of lifetime lead exposure and stress: behavioral, neurochemical and HPA axis effects. *Neurotoxicology* 32 (1):83-99.
122. Virgolini, M.B., A. Rossi-George, R. Lisek, D.D. Weston, M. Thiruchelvam, and D.A. Cory-Slechta. 2008. CNS effects of developmental Pb exposure are enhanced by combined maternal and offspring stress. *Neurotoxicology* 29 (5):812-27.
123. Gump, B.B., Q. Wu, A.K. Dumas, and K. Kannan. 2011. Perfluorochemical (PFC) exposure in children: associations with impaired response inhibition. *Environmental Science & Technology* 45 (19):8151-9.

124. Hoffman, K., T.F. Webster, M.G. Weisskopf, J. Weinberg, and V.M. Vieira. 2010. Exposure to polyfluoroalkyl chemicals and attention deficit/hyperactivity disorder in U.S. children 12-15 years of age. *Environmental Health Perspectives* 118 (12):1762-7.
125. Stein, C.R., and D.A. Savitz. 2011. Serum perfluorinated compound concentration and attention deficit/hyperactivity disorder in children aged 5 to 18 years. *Environmental Health Perspectives* 119 (10):1466-71.
126. Cheuk, D.K., and V. Wong. 2006. Attention-deficit hyperactivity disorder and blood mercury level: a case-control study in Chinese children. *Neuropediatrics* 37 (4):234-40.
127. Julvez, J., F. Debes, P. Weihe, A. Choi, and P. Grandjean. 2010. Sensitivity of continuous performance test (CPT) at age 14 years to developmental methylmercury exposure. *Neurotoxicology and Teratology* 32 (6):627-632.
128. Plusquellec, P., G. Muckle, E. Dewailly, P. Ayotte, G. Begin, C. Desrosiers, C. Despres, D. Saint-Amour, and K. Poitras. 2010. The relation of environmental contaminants exposure to behavioral indicators in Inuit preschoolers in Arctic Quebec. *Neurotoxicology* 31 (1):17-25.
129. National Dissemination Center for Children with Disabilities. 2010. *Disability Fact Sheet-No. 7: Learning Disabilities*. Retrieved April 6, 2010 from <http://www.nichcy.org/InformationResources/Documents/NICHCY%20PUBS/fs7.pdf>.
130. National Center for Learning Disabilities. 2010. *LD at a Glance*. Retrieved April 6, 2010 from <http://www.ncl.org/ld-basics/ld-explained/basic-facts/learning-disabilities-at-a-glance>.
131. Bellinger, D.C. 2008. Very low lead exposures and children's neurodevelopment. *Current Opinion in Pediatrics* 20 (2):172-177.
132. Marlowe, M., A. Cossairt, K. Welch, and J. Errera. 1984. Hair mineral content as a predictor of learning disabilities. *Journal of Learning Disabilities* 17 (7):418-21.
133. Pihl, R.O., and M. Parkes. 1977. Hair element content in learning disabled children. *Science* 198 (4313):204-6.
134. Leviton, A., D. Bellinger, E.N. Allred, M. Rabinowitz, H. Needleman, and S. Schoenbaum. 1993. Pre- and postnatal low-level lead exposure and children's dysfunction in school. *Environmental Research* 60 (1):30-43.
135. Lyngbye, T., O.N. Hansen, A. Trillingsgaard, I. Beese, and P. Grandjean. 1990. Learning disabilities in children: significance of low-level lead-exposure and confounding factors. *Acta Paediatrica Scandinavica* 79 (3):352-60.
136. Needleman, H.L., C. Gunnoe, A. Leviton, R. Reed, H. Peresie, C. Maher, and P. Barrett. 1979. Deficits in psychologic and classroom performance of children with elevated dentine lead levels. *New England Journal of Medicine* 300 (13):689-95.
137. Needleman, H.L., A. Schell, D.C. Bellinger, A. Leviton, and E.N. Allred. 1990. The long term effects of exposure to low doses of lead in childhood, an 11-year follow-up report. *New England Journal of Medicine* 322 (2):83-8.
138. Anderko, L., J. Braun, and P. Auinger. 2010. Contribution of tobacco smoke exposure to learning disabilities. *Journal of Obstetric, Gynecologic, & Neonatal Nursing* 39 (1):111-117.
139. Centers for Disease Control and Prevention. 2010. *Autism Spectrum Disorders: Signs & Symptoms*. Retrieved March 25, 2010 from <http://www.cdc.gov/ncbddd/autism/signs.html>.
140. Beaudet, A.L. 2007. Autism: highly heritable but not inherited. *Nature Medicine* 13 (5):534-6.
141. Hallmayer, J., S. Cleveland, A. Torres, J. Phillips, B. Cohen, T. Torigoe, J. Miller, A. Fedele, J. Collins, K. Smith, et al. 2011. Genetic heritability and shared environmental factors among twin pairs with autism. *Archives of General Psychiatry* 68 (11):1095-102.

142. Levy, D., M. Ronemus, B. Yamrom, Y.-h. Lee, A. Leotta, J. Kendall, S. Marks, B. Lakshmi, D. Pai, K. Ye, et al. 2011. Rare de novo and transmitted copy-number variation in autistic spectrum disorders. *Neuron* 70 (5):886-897.
143. King, M., and P. Bearman. 2009. Diagnostic change and the increased prevalence of autism. *International Journal of Epidemiology* 38 (5):1224-1234.
144. King, M.D., C. Fountain, D. Dakhallah, and P.S. Bearman. 2009. Estimated autism risk and older reproductive age. *American Journal of Public Health* 99 (9):1673-1679.
145. Liu, K.Y., M. King, and P.S. Bearman. 2010. Social influence and the autism epidemic. *American Journal of Sociology* 115 (5):1387-434.
146. Shelton, J.F., D.J. Tancredi, and I. Hertz-Picciotto. 2010. Independent and dependent contributions of advanced maternal and paternal ages to autism risk. *Autism Research* 3 (1):30-9.
147. Pessah, I.N., R.F. Seegal, P.J. Lein, J. LaSalle, B.K. Yee, J. Van De Water, and R.F. Berman. 2008. Immunologic and neurodevelopmental susceptibilities of autism. *Neurotoxicology* 29 (3):532-45.
148. Newschaffer, C.J., L.A. Croen, J. Daniels, E. Giarelli, J.K. Grether, S.E. Levy, D.S. Mandell, L.A. Miller, J. Pinto-Martin, J. Reaven, et al. 2007. The epidemiology of autism spectrum disorders. *Annual Review of Public Health* 28:235-58.
149. Sanders, S.J., A.G. Ercan-Sencicek, V. Hus, R. Luo, M.T. Murtha, D. Moreno-De-Luca, S.H. Chu, M.P. Moreau, A.R. Gupta, S.A. Thomson, et al. 2011. Multiple Recurrent De Novo CNVs, Including Duplications of the 7q11.23 Williams Syndrome Region, Are Strongly Associated with Autism. *Neuron* 70 (5):863-85.
150. Sebat, J., B. Lakshmi, D. Malhotra, J. Troge, C. Lese-Martin, T. Walsh, B. Yamrom, S. Yoon, A. Krasnitz, J. Kendall, et al. 2007. Strong association of de novo copy number mutations with autism. *Science* 316 (5823):445-9.
151. Kinney, D.K., D.H. Barch, B. Chayka, S. Napoleon, and K.M. Munir. 2010. Environmental risk factors for autism: do they help cause de novo genetic mutations that contribute to the disorder? *Medical Hypotheses* 74 (1):102-6.
152. James, S.J., P. Cutler, S. Melnyk, S. Jernigan, L. Janak, D.W. Gaylor, and J.A. Neubrandner. 2004. Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism. *American Journal of Clinical Nutrition* 80 (6):1611-7.
153. James, S.J., S. Melnyk, S. Jernigan, M.A. Cleves, C.H. Halsted, D.H. Wong, P. Cutler, K. Bock, M. Boris, J.J. Bradstreet, et al. 2006. Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics* 141B (8):947-56.
154. Deth, R., C. Muratore, J. Benzecry, V.A. Power-Charnitsky, and M. Waly. 2008. How environmental and genetic factors combine to cause autism: A redox/methylation hypothesis. *Neurotoxicology* 29 (1):190-201.
155. Croen, L.A., D.V. Najjar, B. Fireman, and J.K. Grether. 2007. Maternal and paternal age and risk of autism spectrum disorders. *Archives of Pediatric & Adolescent Medicine* 161 (4):334-40.
156. Grether, J.K., M.C. Anderson, L.A. Croen, D. Smith, and G.C. Windham. 2009. Risk of autism and increasing maternal and paternal age in a large North American population. *American Journal of Epidemiology* 170 (9):1118-26.
157. Lauritsen, M.B., C.B. Pedersen, and P.B. Mortensen. 2005. Effects of familial risk factors and place of birth on the risk of autism: a nationwide register-based study. *Journal of Child Psychology and Psychiatry* 46 (9):963-71.
158. Chandley, A.C. 1991. On the parental origin of de novo mutation in man. *Journal of Medical Genetics* 28 (4):217-23.
159. Crow, J.F. 2000. The origins, patterns and implications of human spontaneous mutation. *Nature Reviews Genetics* 1 (1):40-7.

160. Adams, J.B., J. Romdalvik, V.M. Ramanujam, and M.S. Legator. 2007. Mercury, lead, and zinc in baby teeth of children with autism versus controls. *Journal of Toxicology and Environmental Health A* 70 (12):1046-51.
161. Bradstreet, J., D.A. Geier, J.J. Kartzinel, J.B. Adams, and M.R. Feier. 2003. A case-control study of mercury burden in children with autistic spectrum disorders. *Journal of American Physicians and Surgeons* 8 (3).
162. Desoto, M.C., and R.T. Hitlan. 2007. Blood levels of mercury are related to diagnosis of autism: a reanalysis of an important data set. *Journal of Child Neurology* 22 (11):1308-11.
163. Hertz-Picciotto, I., P.G. Green, L. Delwiche, R. Hansen, C. Walker, and I.N. Pessah. 2010. Blood mercury concentrations in CHARGE Study children with and without autism. *Environmental Health Perspectives* 118 (1):161-6.
164. Palmer, R.F., S. Blanchard, and R. Wood. 2009. Proximity to point sources of environmental mercury release as a predictor of autism prevalence. *Health Place* 15 (1):18-24.
165. Centers for Disease Control and Prevention. *Mercury and Thimerosal: Vaccine Safety*. CDC. Retrieved October 12, 2010 from <http://www.cdc.gov/vaccinesafety/Concerns/thimerosal/index.html>.
166. Institute of Medicine. 2004. *Immunization Safety Review: Vaccines and Autism*. Washington, DC: National Academies Press. [http://www.nap.edu/catalog.php?record\\_id=10997](http://www.nap.edu/catalog.php?record_id=10997).
167. Kalkbrenner, A.E., J.L. Daniels, J.-C. Chen, C. Poole, M. Emch, and J. Morrissey. 2010. Perinatal Exposure to Hazardous Air Pollutants and Autism Spectrum Disorders at Age 8. *Epidemiology* 21 (5):631-41.
168. Windham, G.C., L. Zhang, R. Gunier, L.A. Croen, and J.K. Grether. 2006. Autism spectrum disorders in relation to distribution of hazardous air pollutants in the San Francisco Bay area. *Environmental Health Perspectives* 114 (9):1438-44.
169. Volk, H.E., I. Hertz-Picciotto, L. Delwiche, F. Lurmann, and R. McConnell. 2011. Residential Proximity to Freeways and Autism in the CHARGE Study. *Environmental Health Perspectives* 119 (6):873-7.
170. Larsson, M., B. Weiss, S. Janson, J. Sundell, and C.G. Bornehag. 2009. Associations between indoor environmental factors and parental-reported autistic spectrum disorders in children 6-8 years of age. *Neurotoxicology* 30 (5):822-31.
171. American Association of Intellectual and Developmental Disabilities. 2009. *FAQ on Intellectual Disability*. Retrieved March 23, 2009 from [http://www.aamr.org/content\\_104.cfm?navID=22](http://www.aamr.org/content_104.cfm?navID=22).
172. Schroeder, S.R. 2000. Mental retardation and developmental disabilities influenced by environmental neurotoxic insults. *Environmental Health Perspectives* 108 (Suppl. 3):395-9.
173. Daily, D.K., H.H. Ardinger, and G.E. Holmes. 2000. Identification and evaluation of mental retardation. *American Family Physician* 61 (4):1059-67, 1070.
174. Flint, J., and A.O. Wilkie. 1996. The genetics of mental retardation. *British Medical Bulletin* 52 (3):453-64.
175. Murphy, C., C. Boyle, D. Schendel, P. Decouflé, and M. Yeargin-Allsopp. 1998. Epidemiology of mental retardation in children. *Mental Retardation and Developmental Disabilities Research Reviews* 4 (1):6-13.
176. Bakir, F., H. Rustam, S. Tikriti, S.F. Al-Damluji, and H. Shihristani. 1980. Clinical and epidemiological aspects of methylmercury poisoning. *Postgraduate Medical Journal* 56 (651):1-10.
177. David, O., S. Hoffman, B. McGann, J. Sverd, and J. Clark. 1976. Low lead levels and mental retardation. *Lancet* 2 (8000):1376-9.
178. McDermott, S., J. Wu, B. Cai, A. Lawson, and C. Marjorie Aelion. 2011. Probability of intellectual disability is associated with soil concentrations of arsenic and lead. *Chemosphere* 84 (1):31-8.
179. U.S. Environmental Protection Agency. 2006. *Air Quality Criteria for Lead (Final Report)*. Washington, DC: U.S. EPA, National Center for Environmental Assessment. EPA/600/R-05/144aF-bF. <http://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=158823>.

180. Edwards, S.C., W. Jedrychowski, M. Butscher, D. Camann, A. Kieltyka, E. Mroz, E. Flak, Z. Li, S. Wang, V. Rauh, et al. 2010. Prenatal exposure to airborne polycyclic aromatic hydrocarbons and children's intelligence at age 5 in a prospective cohort study in Poland. *Environmental Health Perspectives* 118 (9):1326-31.
181. Fewtrell, L.J., A. Pruss-Ustun, P. Landrigan, and J.L. Ayuso-Mateos. 2004. Estimating the global burden of disease of mild mental retardation and cardiovascular diseases from environmental lead exposure. *Environmental Research* 94 (2):120-33.
182. U.S. Environmental Protection Agency. 1997. *The Benefits and Costs of the Clean Air Act, 1970 to 1990*. Washington, DC: U.S. EPA, Office of Air and Radiation. <http://www.epa.gov/air/sect812/copy.html>.
183. Weiss, B. 2000. Vulnerability of children and the developing brain to neurotoxic hazards. *Environmental Health Perspectives* 108 (Suppl. 3):375-81.
184. De Los Reyes, A., and A.E. Kazdin. 2005. Informant discrepancies in the assessment of childhood psychopathology: a critical review, theoretical framework, and recommendations for further study. *Psychological Bulletin* 131 (4):483-509.
185. Owens, P.L., K. Hoagwood, S.M. Horwitz, P.J. Leaf, J.M. Poduska, S.G. Kellam, and N.S. Ialongo. 2002. Barriers to children's mental health services. *Journal of the American Academy of Child and Adolescent Psychiatry* 41 (6):731-8.
186. U.S. Department of Health and Human Services. 1999. *Mental Health: A Report of the Surgeon General—Executive Summary*. Rockville, MD: U.S. DHS, Substance Abuse and Mental Health Services Administration, Center for Mental Health Services, National Institutes of Health, National Institute of Mental Health. <http://www.surgeongeneral.gov/library/mentalhealth/pdfs/ExSummary-Final.pdf>.
187. Centers for Disease Control and Prevention. 2007. Prevalence of autism spectrum disorders---autism and developmental disabilities monitoring network, 14 sites, United States, 2002. In: *Surveillance Summaries. Morbidity and Mortality Weekly Report* 56 (No. SS-1):12-28.
188. Kogan, M.D., S.J. Blumberg, L.A. Schieve, C.A. Boyle, J.M. Perrin, R.M. Ghandour, G.K. Singh, B.B. Strickland, E. Trevathan, and P.C. van Dyck. 2009. Prevalence of parent-reported diagnosis of autism spectrum disorder among children in the US, 2007. *Pediatrics* 124 (5):1395-403.