

# PEDIATRICS®

## **Trends in Environmentally Related Childhood Illnesses**

Tracey J. Woodruff, Daniel A. Axelrad, Amy D. Kyle, Onyemaechi Nweke, Gregory

G. Miller and Bradford J. Hurley

*Pediatrics* 2004;113;1133-1140

DOI: 10.1542/peds.113.4.S1.1133

**This information is current as of July 14, 2005**

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://www.pediatrics.org/cgi/content/full/113/4/S1/1133>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2004 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



# Trends in Environmentally Related Childhood Illnesses

Tracey J. Woodruff, PhD, MPH\*; Daniel A. Axelrad, MPP‡; Amy D. Kyle, PhD, MPH§; Onyemaechi Nweke, MPH‡; Gregory G. Miller, MS‡; and Bradford J. Hurley, BA||

**ABSTRACT.** Tracking incidence or prevalence of diseases and using that information to target interventions is a well-established strategy for improving public health. The need to track environmentally mediated chronic diseases is increasingly recognized. Trends in childhood illnesses are 1 element of a framework for children's environmental health indicators, which also includes trends in contaminants in the environment and in concentrations of contaminants in bodies of children and their mothers. This article presents data on 3 groups of important childhood diseases or disorders that seem to be caused or exacerbated, at least in part, by exposure to environmental agents and for which nationally representative data are available. They are asthma, childhood cancers, and neurodevelopmental disorders. Data were used from the National Health Interview Survey for asthma and neurodevelopmental disorders; the Surveillance, Epidemiology, and End Results Program for childhood cancer incidence; and the National Vital Statistics System for childhood cancer mortality. The prevalence of children with asthma doubled between 1980 and 1995, from 3.6% in 1980 to 7.5% in 1995. The annual incidence of childhood cancer increased from 1975 until approximately 1990 and seems to have become fairly stable since. Childhood cancer mortality has declined substantially during the past 25 years. Incidence of certain types of cancers has increased since 1974, including acute lymphoblastic leukemia, central nervous system tumors, and non-Hodgkin's lymphoma. Approximately 6.7% of children aged 5 to 17 were reported to have attention-deficit/hyperactivity disorder in 1997–2000, and approximately 6 of every 1000 children were reported to have received a diagnosis of mental retardation during the same period. *Pediatrics* 2004;113:1133–1140; *children, environmental health, tracking, surveillance, illness, asthma, cancer.*

ABBREVIATIONS. NHIS, National Health Interview Survey; ADHD, attention-deficit/hyperactivity disorder; PCB, polychlorinated biphenyl.

From the \*United States Environmental Protection Agency, San Francisco, California; ‡United States Environmental Protection Agency, Washington, DC; §School of Public Health, University of California, Berkeley, California; and ||ICF Consulting, Washington, DC.

Received for publication Oct 7, 2003; accepted Oct 20, 2003.

Reprint requests to (T.J.W.) Environmental Protection Agency, 75 Hawthorne St, (SPE-1), San Francisco, CA 94105. E-mail: woodruff.tracey@epa.gov

The views expressed in this article are those of the authors and do not necessarily represent those of the US Environmental Protection Agency. PEDIATRICS (ISSN 0031 4005). Copyright © 2004 by the American Academy of Pediatrics.

Tracking the incidence or prevalence of diseases and using that information to target interventions is a well-established strategy for improving public health. Although tracking (or surveillance) approaches have been applied more commonly to infectious diseases, the need to track environmentally mediated chronic diseases is increasingly recognized,<sup>1</sup> particularly as unexplained increases in important diseases are being noted.<sup>2</sup> Tracking can provide data that can be used in research and can lead to identification of hypotheses for detailed investigation. Tracking can also be used to identify opportunities and needs for interventions or policy changes.<sup>3</sup>

This article presents data on 3 groups of important childhood diseases or disorders that seem to be caused or worsened, at least in part, by exposure to environmental agents and for which nationally representative data are available: asthma, cancers, and neurodevelopmental disorders. A framework for environmental public health tracking would address the full pathway from environment to disease and would track releases of contaminants, ambient concentrations, and human exposures, as well as adverse outcomes. One step necessary to develop such a framework is to identify the diseases that should be included and to determine the existing data sources that are available for them. Identification of these outcomes and analysis of the available data are part of a larger national effort to develop concrete, quantifiable measures of children's environment health.<sup>4,5</sup>

## SELECTION OF MEASURES AND DATA SOURCES

The following criteria were used to select childhood illnesses for this analysis: 1) importance to the health of children, 2) availability of data for much or all of the United States, 3) sufficient quality of data to generate reliable results, and 4) published research showing an established or suggested link between environmental contaminants and the illnesses. The groups of illnesses identified as meeting these criteria were asthma, childhood cancer, and certain neurodevelopmental disorders. The data sources used were the National Health Interview Survey (NHIS) for asthma and neurodevelopmental disorders<sup>6,7</sup>; the Surveillance, Epidemiology, and End Results Program for childhood cancer incidence<sup>8</sup>; and the National Vital Statistics System for childhood cancer mortality (Table 1).<sup>9</sup>

**TABLE 1.** Description of Data Sources for the National Data Used Here for Asthma, Cancer, ADHD, and Mental Retardation

Outcome	Years Available	Data Source	Data Description	Notes
Asthma	1980–2000	Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey	Data for ages 0–17. The NHIS is a continuing nationwide sample survey of the civilian noninstitutionalized population collected by personal household interviews. In 2000, 32 374 people 18 years or older and 13 376 children aged 0–17 were interviewed. Data are based on parental response to whether child has had asthma in last 12 months (see text).	
ADHD	1997–2000	Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey	See NHIS description above. Data for ages 5–17. Terminology for this condition has evolved. The American Psychiatric Association adopted the name “attention deficit disorder” in early 1980s and revised it to “attention-deficit/hyperactivity disorder” in 1987. <sup>75</sup> The NHIS of 1997–2000 used here to represent prevalence of ADHD used the term “attention deficit disorder.” Data are based on parental response to the question, “Has a doctor or health professional ever told you that <child’s name> had attention deficit disorder?”	Data for 1997–2000 are combined because of small response in single years. Data for children aged 5–17 are used because of difficulty in diagnosing ADHD in younger children.
Mental retardation	1997–2000	Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey	See NHIS description above. Data for ages 0–17. Data are based on parental response to the question, “Has a doctor or health professional ever told you that <child’s name> had mental retardation?”	Most common definitions emphasize subaverage intellectual functioning before 18 years of age, usually defined as IQ <70, and impairments in life skills. Different severity categories, ranging from mild retardation to severe retardation, are defined by IQ scores. <sup>66</sup>
Childhood cancer	1974–1998	National Cancer Institute; Surveillance, Epidemiology and End Results Program (incidence); Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System (mortality).	Data for ages 0–19. Population-based data used for incidence of cancer that includes information from 5 states and 5 metropolitan areas accounting for approximately 14% of the US population. This is a reasonably representative subset of the US population.	All rates are age-adjusted to the 1970 US standard population.

## CHILDHOOD ILLNESSES

### Asthma

Asthma is the most common chronic disease among children and is costly in both human and monetary terms.<sup>10</sup> In 1994–1996, 24% of children with asthma had to limit their activities as a result of the disease, and asthma caused children to miss 14 million days of school.<sup>11</sup> Asthma prevalence approximately doubled between 1980 and 1995 in the United States.<sup>4,5</sup> The tendency to develop asthma can be inherited, but genetic factors are unlikely to explain the significant increases that have occurred in the past 20 years.<sup>10</sup>

It is well established that several environmental pollutants that are found outdoors and indoors exacerbate asthma. Certain environmental factors may also contribute to the development of asthma. Expo-

sure to dust mites has been identified as a cause of asthma, and exposure to cockroaches and tobacco smoke have been identified as probable causes of asthma.<sup>10</sup> Although research is limited, there is some evidence that indoor air pollutants such as nitrogen dioxide, pesticides, plasticizers, and volatile organic pollutants may also play a role in asthma.<sup>10</sup> Several recent studies suggest that chronic exposure to ozone may be associated with the development of asthma in children who exercise outside and that chronic exposure to particulate matter may affect lung function, growth, and development.<sup>12–14</sup> One study found that exposure to hazardous air pollutants is linked to increases in chronic respiratory symptoms characteristic of asthma.<sup>15</sup>

Children who already have asthma are sensitive to outdoor air pollutants, including ozone, particulate

matter, and sulfur dioxide.<sup>16–29</sup> These pollutants can exacerbate asthma, leading to difficulty in breathing and increases in the use of medication, visits to doctors' offices, trips to emergency departments, and admissions to the hospital.

Figure 1 presents trends in asthma prevalence for children in the United States since 1980. The prevalence of children with asthma doubled between 1980 and 1995, from 3.6% in 1980 to 7.5% in 1995. Asthma prevalence decreased between 1995 and 1996.

Asthma is a complex disease that can be difficult to differentiate from other wheezing disorders, especially in children younger than 6 years. This feature makes it difficult to obtain an accurate measurement of how many children have asthma. Methods used in the NHIS to estimate the prevalence of asthma changed in 1997. Before 1997, children with asthma were identified by asking parents whether a child in their family had asthma during the previous 12 months. In 1997–2000, a parent was asked whether his or her child had ever received a diagnosis of asthma by a health professional. If the parent answered yes, then he or she was asked whether the child had had an asthma attack or episode in the previous 12 months. The percentage of children with an asthma attack in the last 12 months measures the population with incomplete control of asthma and sometimes is referred to as "attack prevalence." Starting in 2001, the NHIS included a question that allows the estimation of the percentage of children who currently have asthma. In 2001, 8.7 percent (6.3 million) of children had asthma.

### Childhood Cancer

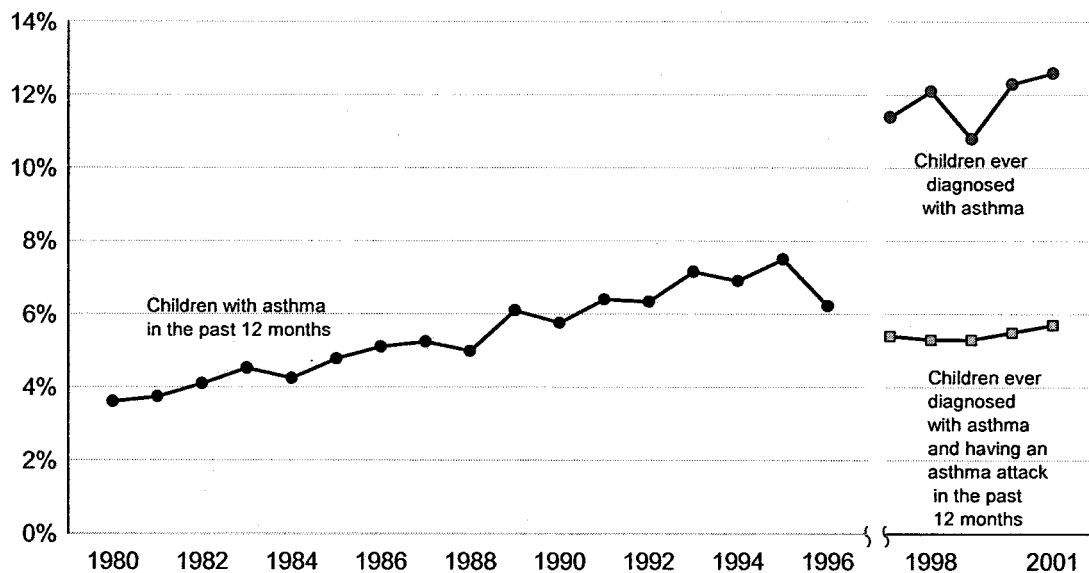
Although cancer in childhood is rare compared with cancer in adults, it is the second most common cause of death, after injuries and accidents, among

children 1 to 19 years of age.<sup>30</sup> The annual incidence of childhood cancer increased from 1975 until approximately 1990 and seems to have become fairly stable since 1990. There are differing analyses on how much of the increase is a real increase or is from diagnostic improvements or reporting changes.<sup>31,32</sup> One aspect that has not been considered in these analyses is underreporting as a result of reporting delay and reporting errors, which has been found to be significant in trends for adult cancers.<sup>33</sup> In either case, it is critically important to monitor trends to assess whether there are increases or decreases of this important disease. Mortality has declined substantially during the past 25 years, largely as a result of improvements in treatment (Fig 2).<sup>30</sup>

Trends in incidence of all forms of childhood cancer combined may be useful for assessing the overall burden of cancer among children. However, incidence of individual cancers varies considerably. Moreover, environmental chemicals have been more closely linked to some childhood cancers than to others. Children may be particularly susceptible to exposures in utero or during early life because the fetus or young child's physiology is undergoing rapid development, such as rapid cell division, changing metabolic activity, and evolving hormonal systems.<sup>34</sup> Figure 3 shows the trends in cancer incidence by type for the 4 most common childhood cancers. An accompanying article in this supplement by Miller discusses the potential role of environmental contaminants and childhood cancer.

### Neurodevelopmental Disorders

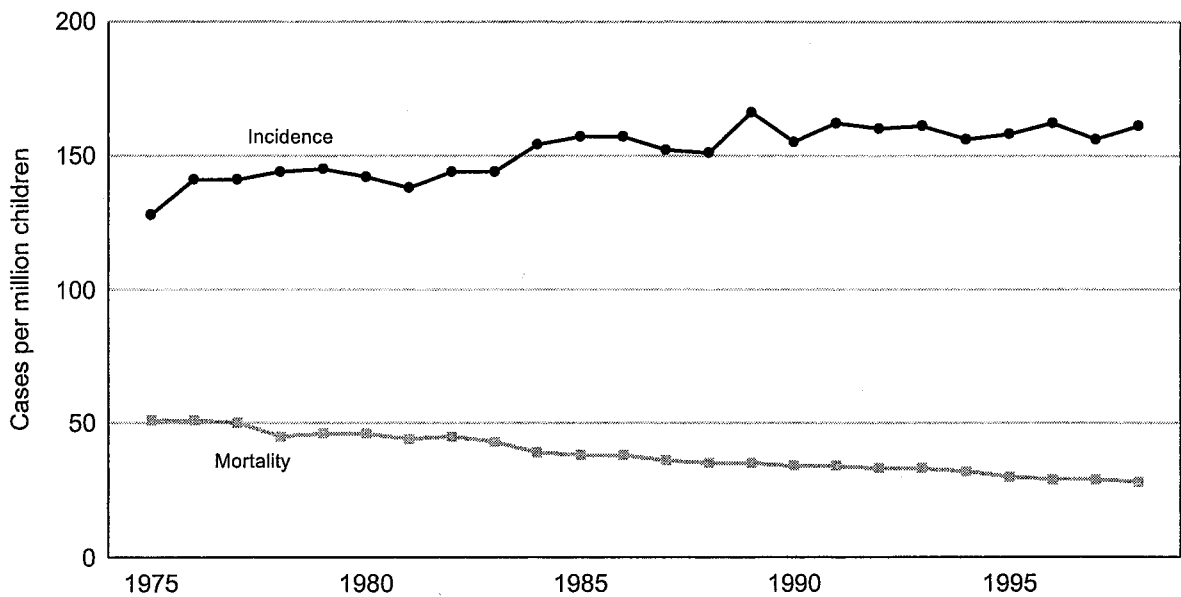
Researchers estimate that between 3% and 8% of the infants born each year in the United States are or will be affected by neurodevelopmental disorders such as attention-deficit/hyperactivity disorder



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

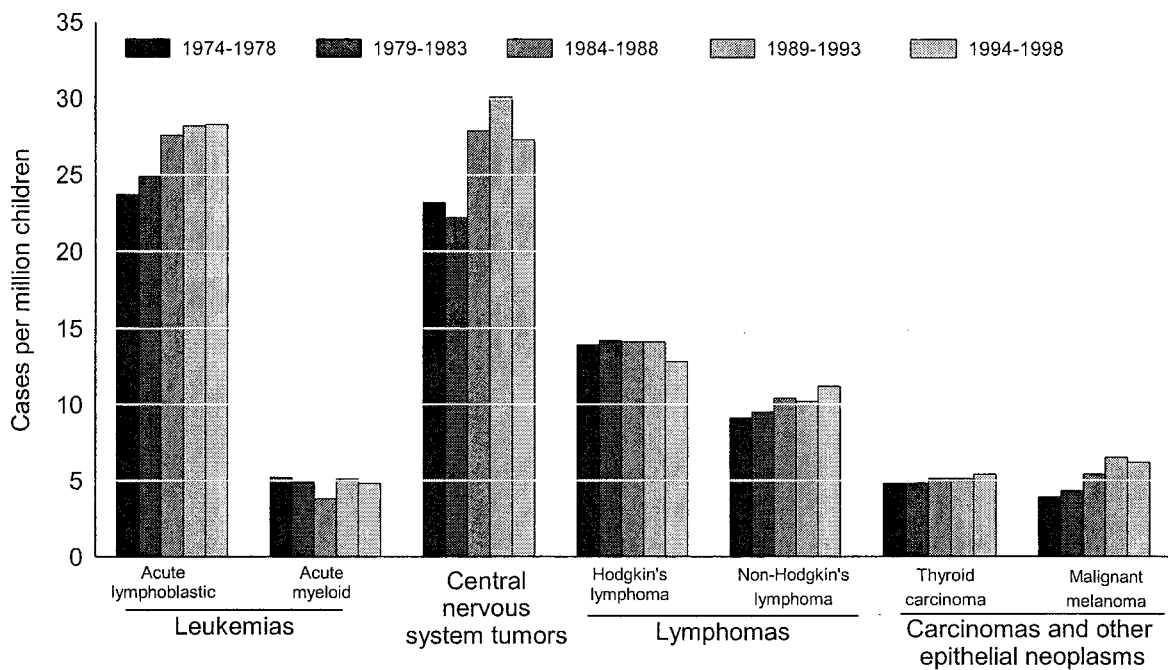
Note: The survey questions for asthma changed in 1997; data before 1997 cannot be directly compared to data in 1997 and later.

Fig 1. Percentage of children with asthma, 1980–2001.



SOURCE: Incidence data from National Cancer Institute, Surveillance, Epidemiology and End Results Program; mortality data from Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System

Fig 2. Childhood cancer incidence and mortality for children under 20, 1974–1998.



SOURCE: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance, Epidemiology, and End Results Program

Fig 3. Childhood cancer by type for children under 20, 1974–1998.

(ADHD), mental retardation, or autism.<sup>35</sup> Neurodevelopmental disorders may result from exposure of the fetus or young child to environmental contaminants. A child's brain is vulnerable to adverse impacts from some environmental toxicants during its developmental process.<sup>36,37</sup> Causes of neurodevelopmental disorders are unknown in the majority of cases.<sup>35</sup>

Lead, methylmercury, polychlorinated biphenyls

(PCBs), and other widely distributed environmental contaminants have been shown to damage children's developing brains and nervous systems. Exposure to lead during childhood reduces intelligence and affects cognitive development.<sup>38–40</sup> Studies also have found that childhood exposure to lead contributes to ADHD<sup>41</sup> and hyperactivity and distractibility<sup>42–44</sup>; increases the likelihood of dropping out of high school and having a reading disability, reduced vo-

cabulary, and lower class standing in high school<sup>45</sup>; and increases the risk for antisocial and delinquent behavior.<sup>46</sup>

Methylmercury also negatively affects children's neurologic development. Studies of methylmercury exposure in utero found adverse impacts on intelligence<sup>47,48</sup> and decreased functioning in language, attention, and memory.<sup>49</sup> Particularly high levels of mercury exposure in utero cause mental retardation.<sup>50,51</sup>

Several studies link neurodevelopmental effects to elevated levels of PCBs, including lowered intelligence and behavioral deficits such as inattention and excessive reaction to stimulation. Most of these studies find effects associated with exposure in utero resulting from the mother's having eaten food contaminated with PCBs.<sup>52-57</sup> Adverse effects on intelligence and behavior also have been found in children of mothers who were highly exposed to mixtures of PCBs, chlorinated dibenzofurans, and other pollutants before conception.<sup>58-60</sup> There is suggestive evidence from animal and human studies indicating some potential for adverse effects on neurologic development for metals such as cadmium and arsenic,<sup>42,61-63</sup> organophosphate pesticides,<sup>64</sup> and some brominated flame retardants.<sup>65</sup>

This article presents 2 neurodevelopmental outcomes that may be related partly to environmental contaminant exposures: ADHD and mental retardation.

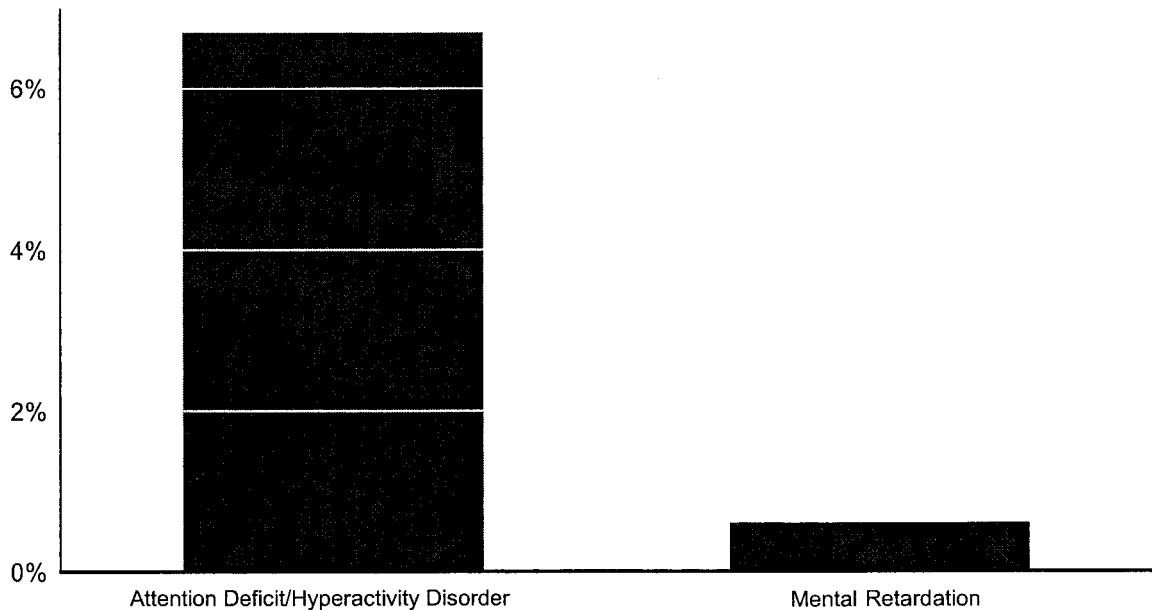
#### ADHD

ADHD is defined as impairment in functioning associated with multiple symptoms of inattention to tasks or instructions, hyperactivity, and impulsivity.<sup>66</sup>

It can make family and peer relationships difficult, diminish academic performance, and reduce vocational development.

The causes of ADHD are unknown. Few studies have looked explicitly at the relationship between ADHD and exposures to environmental contaminants. However, evidence supports a hypothesis that environmental contaminants may contribute to some portion of the incidence of ADHD, based on inference from studies focusing on specific symptoms or types of behavior associated with ADHD. As noted above, studies have found relationships between behavioral problems—including attention problems, hyperactivity, and impulsivity—and exposures to lead<sup>42-46,67</sup> and PCBs.<sup>53-56</sup> Such behavioral problems, in their more severe forms, may result in a diagnosis of ADHD. Animal studies also provide supporting evidence that exposures to PCBs and lead may contribute to ADHD.<sup>67,68</sup>

Approximately 6.7% of children aged 5 to 17 were reported to have ADHD in 1997-2000 (Fig 4). Although these data from the NHIS are the best available national data, it is difficult to estimate the prevalence of ADHD. Unlike illnesses such as cancer, diagnosis of ADHD and other psychiatric disorders relies on recognition of various types of behaviors in different combinations, and therefore requires a great deal of judgment. Also, a diagnosis of ADHD may depend on whether a parent or a teacher raises concerns about a child's behavior. Furthermore, cultural factors may influence the way a child's behavior is labeled and diagnosed. In addition, the NHIS relies on parents' reporting their child's diagnosis of ADHD, and accuracy of parental responses may be influenced by a variety of factors.



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

Fig 4. Percentage of children aged 5 to 17 reported to have ADHD and children aged 0 to 17 reported to have mental retardation, 1997-2000.

ADHD data are available from the NHIS only for the years 1997–2000, which does not provide a sufficient basis for detecting whether there has been any increase or decrease in ADHD over time. Although more children recently have received a diagnosis of and been treated for ADHD, this increase may be attributable in part to greater awareness of the condition, development of effective treatments, or other factors.

#### Mental Retardation

Researchers have identified many causes of mental retardation, including genetic disorders, traumatic accidents, and prenatal events such as maternal infection or exposure to alcohol.<sup>69,70</sup> Exposure to lead and exposure to particularly high levels of mercury also have been shown to cause mental retardation.<sup>50,51,71</sup> Furthermore, lead, mercury, and PCBs all have been found to have adverse effects on intelligence and cognitive functioning. Any contaminant with such effects has potential to increase the incidence of mental retardation in an exposed population.<sup>72</sup>

The causes of mental retardation are unknown in 30% to 50% of all cases.<sup>70</sup> The causes are more frequently identified for cases of severe retardation (IQ <50). The cause of mild retardation (IQ between 50 and 70) is unknown in >75% of cases.<sup>73,74</sup> Approximately 6 of every 1000 children were reported to have received a diagnosis of mental retardation in 1997–2000, as shown in Fig 4.

#### DISCUSSION

This article presents data on trends in incidence and prevalence of several important childhood illnesses that may be related in part to environmental pollutants. For asthma and some childhood cancers, the frequency seems to have increased over the last 25 to 30 years. A relatively high percentage of children are affected by ADHD and mental retardation, but the data are insufficient to determine trends. The frequency of these diseases and disorders provides a compelling basis for increased attention to these illnesses and their causes.

This article reflects consideration of 3 groups of diseases. Others may also be relevant to include in future analyses. Certain illnesses not discussed here, such as birth defects and waterborne diseases, may be environmentally mediated. However, nationally representative data are not available for these diseases. Environmental factors also may affect human reproduction, contributing to effects such as earlier age at puberty. Work is ongoing to identify and develop data sources that could provide trend information for these important conditions.

Trends in exposures to environmental contaminants should be evaluated as part of a process to define the role of environmental contaminants in these and other childhood illnesses. For example, data on exposures to environmental contaminants associated with neurodevelopmental disorders in children, such as lead and mercury, should be considered in conjunction with the data on neurodevel-

opmental disorders in children. Additional data on exposures to environmental contaminants that are or may be associated with childhood illnesses are presented and discussed in the Environmental Protection Agency's "America's Children and the Environment" report series.<sup>4,5</sup>

The prevalence of many childhood diseases varies by race/ethnicity and family income. For example, children of lower-income families and children of color are more likely to have had an asthma attack in the previous 12 months than are white children and/or children from higher-income families.<sup>4,5</sup> Evaluating data by race/ethnicity and income can identify groups of children who are at higher risk and contribute to information on health disparities. Data on the incidence of childhood illnesses by race and family income also are available in the "America's Children and the Environment" reports.<sup>4,5</sup>

#### ACKNOWLEDGMENTS

Funding for this research was provided by the National Center for Environmental Economics and the Office of Children's Health Protection, US Environmental Protection Agency.

#### REFERENCES

1. Pew Environmental Health Commission. *America's Environmental Health Gap: Why the Country Needs a Nationwide Health Tracking Network*. Baltimore, MD: Pew Environmental Health Commission, Johns Hopkins School of Hygiene and Public Health; 2000
2. Trust for America's Health. *Short of Breath: Our Lack of Response to the Growing Asthma Epidemic and the Need for Nationwide Tracking*. Washington, DC: Trust for American Health; 2001. Available at: <http://healthyamericans.org/reports/files/shortofbreath.pdf>
3. Thacker SB, Stroup DF, Parrish RG, Anderson HA. Surveillance in environmental public health: issues, systems, and sources. *Am J Public Health*. 1996;86:633–638
4. Woodruff T, Axelrad D, Kyle A, Nweke O, Miller G. *America's Children and the Environment: Measures of Contaminants, Body Burdens, and Illnesses*. Washington, DC: US Environmental Protection Agency; 2003 (Report No. EPA 240-R-03-001). Available at: <http://www.epa.gov/envirohealth/children>
5. Woodruff T, Axelrad D, Kyle A. *America's Children and the Environment: A First View of Available Measures*. Washington, DC: US Environmental Protection Agency; 2000 (Report No. EPA 240-R-00-006)
6. National Center for Health Statistics. *National Health Interview Survey*. Hyattsville, MD: National Center for Health Statistics; 2002
7. Design and estimation for the National Health Interview Survey, 1995–2004. *Vital Health Stat 2*. 2000;(130):1–31
8. National Cancer Institute. *Surveillance, Epidemiology, and End Results*. Bethesda, MD: National Cancer Institute; 2002
9. National Center for Health Statistics. *National Vital Statistics System*. Hyattsville, MD: National Center for Health Statistics; 2002
10. National Academy of Sciences. *Clearing the Air: Asthma and Indoor Air Exposures*. Washington, DC: National Academy Press; 2000
11. Mannino DM, Homa DM, Akinbami LJ, Moorman JE, Gwynn C, Redd SC. Surveillance for Asthma—United States, 1980–1999. *MMWR Morb Mortal Wkly Rep*. 2002;51:1–13
12. Avol EL, Gauderman WJ, Tan SM, London SJ, Peters JM. Respiratory effects of relocating to areas of differing air pollution levels. *Am J Respir Crit Care Med*. 2001;164:2067–2072
13. McConnell R, Berhane K, Gilliland F, et al. Asthma in exercising children exposed to ozone: a cohort study. *Lancet*. 2002;359:386–391
14. Gauderman WJ, Gilliland GF, Vora H, et al. Association between air pollution and lung function growth in southern California children: results from a second cohort. *Am J Respir Crit Care Med*. 2002;166:76–84
15. Ware JH, Spengler JD, Neas LM, et al. Respiratory and irritant health effects of ambient volatile organic compounds. The Kanawha County Health Study. *Am J Epidemiol*. 1993;137:1287–1301
16. Fauroux B, Sampil M, Quénel P, Lemoulléc Y. Ozone: a trigger for hospital pediatric asthma emergency room visits. *Pediatr Pulmonol*. 2000; 30:41–46
17. Hirsch T, Weiland SK, von Mutius E, et al. Inner city air pollution and respiratory health and atopy in children. *Eur Respir J*. 1999;14:669–677

18. Hrubá F, Fabiánová E, Koppová K, Vandenberg JJ. Childhood respiratory symptoms, hospital admissions, and long-term exposure to airborne particulate matter. *J Expo Anal Environ Epidemiol*. 2001;11:33–40
19. Koenig JQ. Air pollution and asthma. *J Allergy Clin Immunol*. 1999;104(suppl):717–722
20. van der Zee S, Hoek G, Boezen HM, Schouten JP, van Wijnen JH, Brunekreef B. Acute effects of urban air pollution on respiratory health of children with and without chronic respiratory symptoms. *Occup Environ Med*. 1999;56:802–812
21. Roemer W, Hoek G, Brunekreef B. Pollution effects on asthmatic children in Europe, the PEACE study. *Clin Exp Allergy*. 2000;30:1067–1075
22. Lipsett M, Hurley S, Ostro B. Air pollution and emergency room visits for asthma in Santa Clara County, California. *Environ Health Perspect*. 1997;105:216–222
23. Norris G, YoungPong SN, Koenig JQ, Larson TV, Sheppard L, Stout JW. An association between fine particles and asthma emergency department visits for children in Seattle. *Environ Health Perspect*. 1999;107:489–493
24. McConnell R, Berhane K, Gilliland F, et al. Air pollution and bronchitic symptoms in Southern California children with asthma. *Environ Health Perspect*. 1999;107:757–760
25. Peters A, Dockery DW, Heinrich J, Wichmann HE. Short-term effects of particulate air pollution on respiratory morbidity in asthmatic children. *Eur Respir J*. 1997;10:872–879
26. US Environmental Protection Agency. *Supplement to the Second Addendum (1986) to Air Quality Criteria for Particulate Matter and Sulfur Oxides: Assessment of New Findings on Sulfur Dioxide Acute Exposure Health Effects in Asthmatic Individuals*. Research Triangle Park, NC: Office of Research and Development; 1994 (Report No. EPA 600/FP-93/002)
27. US Environmental Protection Agency. *Air Quality Criteria for Ozone and Related Photochemical Oxidants*. Washington, DC: National Center for Environmental Assessment, Office of Research and Development; 1996 (Report No. EPA/600/P-93/004aF)
28. US Environmental Protection Agency. *Air Quality Criteria for Particulate Matter*. Washington, DC: National Center for Environmental Assessment, Office of Research and Development; 1996 (Report No. EPA/600/P-95/001aF)
29. Burnett RT, Smith-Doiron M, Stieb D, et al. Association between ozone and hospitalization for acute respiratory diseases in children less than 2 years of age. *Am J Epidemiol*. 2001;153:444–452
30. Reis LAG, Smith MA, Gurney JG, et al. *Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975–1995*. Bethesda, MD: National Cancer Institute, SEER Program; 1999 (Report No. NIH Pub. No. 99-4649)
31. Gurney JG, Davis S, Severson RK, Fang JY, Ross JA, Robison LL. Trends in cancer incidence among children in the U.S. *Cancer*. 1996;78:532–541
32. Linet MS, Ries LA, Smith MA, Tarone RE, Devesa SS. Cancer surveillance series: recent trends in childhood cancer incidence and mortality in the United States. *J Natl Cancer Inst*. 1999;91:1051–1058
33. Clegg LX, Feuer EJ, Midthune DN, Fay MP, Hankey BF. Impact of reporting delay and reporting error on cancer incidence rates and trends. *J Natl Cancer Inst*. 2002;94:1537–1545
34. Anderson LM, Diwan BA, Fear NT, Roman E. Critical windows of exposure for children's health: cancer in human epidemiological studies and neoplasms in experimental animal models. *Environ Health Perspect*. 2000;108(suppl 3):573–594
35. Weiss B, Landrigan PJ. The developing brain and the environment: an introduction. *Environ Health Perspect*. 2000;108(suppl 3):373–374
36. Rice D, Barone S Jr. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. *Environ Health Perspect*. 2000;108(suppl 3):511–533
37. Rodier PM. Developing brain as a target of toxicity. *Environ Health Perspect*. 1995;103(suppl 6):73–76
38. Bellinger DC, Leviton A, Waternaux C. Longitudinal analyses of prenatal and postnatal lead exposure and early cognitive development. *N Engl J Med*. 1987;316:1037–1043
39. McMichael AJ, Baghurst PA, Wigg NR, Vimpani GV, Robertson EF, Roberts RJ. Port Pirie Cohort Study: environmental exposure to lead and children's abilities at the age of four years. *N Engl J Med*. 1988;319:468–475
40. Lanphear BP, Dietrich K, Auinger P, Cox C. Cognitive deficits associated with blood lead concentrations <10 micrograms/dL in U.S. children and adolescents. *Public Health Rep*. 2000;115:521–529
41. Tuthill RW. Hair lead levels related to children's classroom attention-deficit behavior. *Arch Environ Health*. 1996;51:214–220
42. Calderon J, Navarro ME, Jimenez-Capdeville ME, et al. Exposure to arsenic and lead and neuropsychological development in Mexican children. *Environ Res*. 2001;85:69–76
43. Mendelsohn AL, Dreyer BP, Fierman AH, et al. Low-level lead exposure and behavior in early childhood. *Pediatrics*. 1998;101(3). Available at: [pediatrics.org/cgi/content/full/101/3/e10](http://pediatrics.org/cgi/content/full/101/3/e10)
44. Minder B, Das-Smaal EA, Brand EF, Orlebeke JF. Exposure to lead and specific attentional problems in schoolchildren. *J Learn Disabil*. 1994;27:393–399
45. Needleman HL, Schell A, Bellinger DC, Leviton A, Allred EN. The long term effects of exposure to low doses of lead in childhood, an 11-year follow-up report. *N Engl J Med*. 1990;322:83–88
46. Needleman HL, Riess JA, Tobin MJ, Biesecker GE, Greenhouse JB. Bone lead levels and delinquent behavior. *JAMA*. 1996;275:363–369
47. Kjellstrom T, Kennedy P, Wallis P, Mantell C. *Physical and Mental Development of Children With Prenatal Exposure to Mercury From Fish. Stage 2: Interviews and Psychological Tests at Age 6*. Solna, Sweden: National Swedish Environmental Protection Board; 1989 (Report No. 3642)
48. Crump KS, Kjellstrom T, Shipp AM, Silvers A, Stewart A. Influence of prenatal mercury exposure upon scholastic and psychological test performance: benchmark analysis of a New Zealand cohort. *Risk Anal*. 1998;18:701–713
49. Grandjean P, Weihe P, White RF, et al. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicol Teratol*. 1997;19:417–428
50. Harada M, Akagi H, Tsuda T, Kizaki T, Ohno H. Methylmercury level in umbilical cords from patients with congenital Minamata disease. *Sci Tot Environ*. 1999;234:59–62
51. Bakir F, Rustam H, Tikriti S, Al-Damluji SF, Shihristani H. Clinical and epidemiological aspects of methylmercury poisoning. *Postgrad Med J*. 1980;56:1–10
52. Darvill T, Lonky E, Reihman J, Stewart P, Pagano J. Prenatal exposure to PCBs and infant performance on the Fagan test of infant intelligence. *Neurotoxicology*. 2000;21:1029–1038
53. Jacobson JL, Jacobson SW. Intellectual impairment in children exposed to polychlorinated biphenyls in utero. *N Engl J Med*. 1996;335:783–789
54. Jacobson JL, Jacobson SW. Teratogen update: polychlorinated biphenyls. *Teratology*. 1997;55:338–347
55. Patandin S, Lanting CI, Mulder PG, Boersma ER, Sauer PJ, Weisglas-Kuperus N. Effects of environmental exposure to polychlorinated biphenyls and dioxins on cognitive abilities in Dutch children at 42 months of age. *J Pediatr*. 1999;134:33–41
56. Stewart P, Reihman J, Lonky E, Darvill T, Pagano J. Prenatal PCB exposure and neonatal behavioral assessment scale (NBAS) performance. *Neurotoxicol Teratol*. 2000;22:21–29
57. Walkowiak J, Wiener JA, Fastabend A, et al. Environmental exposure to polychlorinated biphenyls and quality of the home environment: effects on psychodevelopment in early childhood. *Lancet*. 2001;358:1602–1607
58. Rogan WJ, Gladen BC, Hung KL, et al. Congenital poisoning by polychlorinated biphenyls and their contaminants in Taiwan. *Science*. 1988;241:334–336
59. Chen YC, Guo YL, Hsu CC, Rogan WJ. Cognitive development of Yu-Cheng ("oil disease") children prenatally exposed to heat-degraded PCBs. *JAMA*. 1992;268:3213–3218
60. Chen YC, Yu ML, Rogan WJ, Gladen BC, Hsu CC. A 6-year follow-up of behavior and activity disorders in the Taiwan Yu-cheng children. *Am J Public Health*. 1994;84:415–421
61. Marlowe M, Cossairt A, Moon C, et al. Main and interaction effects of metallic toxins on classroom behavior. *J Abnorm Child Psychol*. 1985;13:185–198
62. Stewart-Pinkham SM. The effect of ambient cadmium air pollution on the hair mineral content of children. *Sci Tot Environ*. 1989;78:289–296
63. Thatcher RW, Lester ML, McAlaster R, Horst R. Effects of low levels of cadmium and lead on cognitive functioning in children. *Arch Environ Health*. 1982;37:159–166
64. Eskenazi B, Bradman A, Castorina R. Exposures of children to organophosphate pesticides and their potential adverse health effects. *Environ Health Perspect*. 1999;107(suppl 3):409–419
65. Eriksson P, Jakobsson E, Fredriksson A. Brominated flame retardants: a novel class of developmental neurotoxicants in our environment? *Environ Health Perspect*. 2001;109:903–908
66. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994
67. Rice DC. Behavioral effects of lead: commonalities between experimental and epidemiologic data. *Environ Health Perspect*. 1996;104(suppl 2):337–351
68. Rice DC. Parallels between attention deficit hyperactivity disorder and behavioral deficits produced by neurotoxic exposure in monkeys. *Environ Health Perspect*. 2000;108(suppl 3):405–408
69. Schroeder SR. Mental retardation and developmental disabilities influ-



- enced by environmental neurotoxic insults. *Environ Health Perspect.* 2000;108(suppl 3):395–399
70. Daily DK, Ardinger HH, Holmes GE. Identification and evaluation of mental retardation. *Am Fam Physician* 2000;61:1059–1067, 1070
71. David O, Hoffman S, McGann B, Sverd J, Clark J. Low lead levels and mental retardation. *Lancet.* 1976;2:1376–1379
72. Weiss B. Vulnerability of children and the developing brain to neurotoxic hazards. *Environ Health Perspect.* 2000;108(suppl 3):375–381
73. Murphy C, Boyle C, Schendel D, Decouflé P, Yeargin-Allsopp M. Epidemiology of mental retardation in children. *Ment Retard Dev Disabil Res Rev.* 1998;4:6–13
74. Flint J, Wilkie AO. The genetics of mental retardation. *Br Med Bull.* 1996;52:453–464
75. National Institute of Mental Health. *Attention Deficit Hyperactivity Disorder (ADHD)—Questions and Answers.* Bethesda, MD: National Institute of Mental Health; 2000

## Trends in Environmentally Related Childhood Illnesses

Tracey J. Woodruff, Daniel A. Axelrad, Amy D. Kyle, Onyemaechi Nweke, Gregory

G. Miller and Bradford J. Hurley

*Pediatrics* 2004;113;1133-1140

DOI: 10.1542/peds.113.4.S1.1133

**This information is current as of July 14, 2005**

<b>Updated Information &amp; Services</b>	including high-resolution figures, can be found at: <a href="http://www.pediatrics.org/cgi/content/full/113/4/S1/1133">http://www.pediatrics.org/cgi/content/full/113/4/S1/1133</a>
<b>References</b>	This article cites 59 articles, 19 of which you can access for free at: <a href="http://www.pediatrics.org/cgi/content/full/113/4/S1/1133#BIBL">http://www.pediatrics.org/cgi/content/full/113/4/S1/1133#BIBL</a>
<b>Citations</b>	This article has been cited by 1 HighWire-hosted articles: <a href="http://www.pediatrics.org/cgi/content/full/113/4/S1/1133#otherarticles">http://www.pediatrics.org/cgi/content/full/113/4/S1/1133#otherarticles</a>
<b>Post-Publication Peer Reviews (P<sup>3</sup>Rs)</b>	One P <sup>3</sup> R has been posted to this article: <a href="http://www.pediatrics.org/cgi/eletters/113/4/S1/1133">http://www.pediatrics.org/cgi/eletters/113/4/S1/1133</a>
<b>Subspecialty Collections</b>	This article, along with others on similar topics, appears in the following collection(s): <b>Therapeutics &amp; Toxicology</b> <a href="http://www.pediatrics.org/cgi/collection/therapeutics_and_toxicology">http://www.pediatrics.org/cgi/collection/therapeutics_and_toxicology</a>
<b>Permissions &amp; Licensing</b>	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="http://www.pediatrics.org/misc/Permissions.shtml">http://www.pediatrics.org/misc/Permissions.shtml</a>
<b>Reprints</b>	Information about ordering reprints can be found online: <a href="http://www.pediatrics.org/misc/reprints.shtml">http://www.pediatrics.org/misc/reprints.shtml</a>

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

