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The Health and Well-Being of Children from the Perspective of Social and Environmental Health Policy

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ABSTRACT

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Frederica Perera

Environmental health is an integral component of public health and, therefore, of social welfare. Yet both social and environmental health scientists have failed to adequately consider the mutual benefits of --and synergism between-- environmental and social policies aimed at the protection of the health and well-being of children. The emerging scientific evidence that social and physical/chemical ñtoxicantsò interact to cause childhood illness and impair childrenôs development is providing new impetus to the integration of these disciplines.

Child labor reform in the late 19th century can be seen as a milestone in the translation of science to policy. For the first time, scientific recognition of childrenôs biological and psychological vulnerability was a major factor in shaping public policy. Yet the role of science as a force in shaping the perception of the value of the child and as a driver of reform during this period has not been widely recognized. The first paper, entitled ñThe Role of Science in Child Labor Reform in the Early Progressive Era (1870-1900)ò, describes how the growing understanding of physicians, toxicologists, sociologists, and psychologists that childhood was a biologically vulnerable period of life informed progressive reformers who used this knowledge, along with socio-economic, cultural and moral arguments, to advocate for reform.

During the past several decades, there has been an exponential growth in scientific knowledge concerning the biological vulnerability of the developing fetus, infant, and child both to the toxic effects of environmental pollutants <u>and</u> psychosocial stressors associated with poverty or race/ethnicity. However, data are limited on the possible cumulative or synergistic effects of physical and ósocialô toxicants on child health and development. The second paper,

entitled ñInteraction between Prenatal Exposure to Airborne Polycyclic Aromatic Hydrocarbons and Maternal Psychological Distress in Pregnancy on Child Behavior ñ provides new evidence of the complex consequences of environmental exposures acting in conjunction with psychosocial stressors. The specific research question addressed is whether maternal demoralization during pregnancy has a greater effect on neurobehavioral effects manifesting in childhood among children with high exposure to air pollution during gestation compared to those with low exposure. The results indicate the need for a multifaceted approach to prevention of developmental problems in children.

A potential stumbling block to the integration of social and environmental policy has been the lack of adequately detailed analyses of the benefits of reducing environmental pollution. More research is needed on the monetized benefits of reducing pollution, in the overall population and as they affect less advantaged populations. The third paper entitled ñPrenatal Exposure to Airborne Polycyclic Aromatic Hydrocarbons and IQ: Estimated Cost of IQ reductionòaddresses the gap in understanding of the potential economic benefits of reducing environmental pollution and estimates the increase in IQ and related lifetime earnings that would be expected in a low- income urban population as a result of a modest reduction of ambient concentrations of the combustion related pollutants, PAH.

The dissertation presents these three interrelated original papers providing new evidence supporting a broad, integrated policy that addresses environmental degradation and inequality. These three papers stand on their own as original contributions to the field. By addressing three important research gaps, they provide needed evidence to support greater protection of children through an integrated social and environmental policy.

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INTRODUCTION

Environmental health is an integral component of public health and, therefore, of social welfare. Yet it is rarely considered in that dual light, resulting in a failure to consider the mutual benefits of --and synergism between-- environmental and social policies aimed at the protection of the health and well-being of children. An integration of the two is now being forced by the emerging scientific evidence that social and physical/chemical ñtoxicantsò interact to cause childhood illness and impair childrenôs development--much as the emerging science on the biological vulnerability of children contributed to reform of the child labor laws during the Progressive Era.

Child labor reform in the late 19th century can be seen as a milestone in the translation of science to policy. For the first time, scientific recognition of childrenôs biological and psychological vulnerability was a major factor in shaping public policy. The process that led to the New York State Child Labor Law of 1886 is an early example of efforts to put in place a science-based social and environmental policy regarding the protection of childrenôs health and development. Yet the role of science as a force in shaping the perception of the value of the child and as a driver of reform during this period has not been widely recognized.

The first paper, entitled ñThe Role of Science in Child Labor Reform in the Early Progressive Era (1870-1900)ò, describes how the growing understanding of physicians, toxicologists, sociologists, and psychologists that childhood was a biologically vulnerable period of life informed progressive reformers who used this knowledge, along with socio-economic, cultural and moral arguments, to advocate for reform.

During the past several decades, there has been an exponential growth in scientific knowledge concerning the biological vulnerability of the developing fetus, infant, and child both to the toxic effects of environmental pollutants and psychosocial stressors associated with poverty or race/ethnicity (Anderson, Diwan, Fear, & Roman, 2000; Grandjean & Landrigan,

2006; National Research Council, 1993; Perera et al., 2004; Sandman, Davis, Buss, & Glynn, 2012; World Health Organization, 1986). Of special concern are cumulative or synergistic effects of physical and ósocialô toxicants on child health and development because these exposures tend to cluster in the most socially disadvantaged populations (Chen, Schreier, Strunk, & Brauer, 2008; Clougherty et al., 2007; Cohen, Janicki-Deverts, & Miller, 2007; Rauh et al., 2004; Wright, 2009). A number of epidemiologic studies show interactions between income or race and various pollutants (Chuang, Callahan, Lyu, & Wilson, 1999). However, only a few studies exist on interactions between psychosocial factors, and pollutants. These include interactions between prenatal exposure to environmental tobacco smoke and material hardship on cognitive deficits at two years of age (Rauh, et al., 2004) and between neonatal blood lead levels and poverty on cognitive deficits in four year old children (Dietrich, Succop, Berger, Hammond, & Bornschein, 1991).

The second paper, entitled ñInteraction Between Prenatal Exposure to Airborne Polycyclic Aromatic Hydrocarbons and Maternal Psychological Distress in Pregnancy on Child Behavior ñ provides new evidence of the complex consequences of environmental exposures acting in conjunction with psychosocial stressors. The specific research question addressed is whether maternal demoralization during pregnancy has a greater effect on neurobehavioral effects manifesting in childhood among children with high exposure to air pollution during gestation compared to those with low exposure. The results indicate the need for a multifaceted approach to prevention of developmental problems in children.

Perhaps more than social welfare policies, environmental protection has been a magnet for attack as overly costly to society and burdensome to industry. This is a potential stumbling block to the integration of social and environmental policy. There are relatively few adequately detailed cost-benefit analyses due to the limitations of available data. However, in cases where well-conducted cost-benefit analyses are available, such as for particulate air pollution, lead and mercury, the estimated benefits exceed the costs (EPA, 1999; S. D. Grosse, T. D. Matte, J.

Schwartz, & R. J. Jackson, 2002; Trasande, Landrigan, & Schechter, 2005) (EPA, 2011). For example, a 2007 study estimated the total costs of damage associated with emissions of some air pollutants (particulate matter, nitrogen oxides, ammonia, sulphur dioxide, volatile organic compounds) in the U.S. at between US$71 billion and $277 billion per year (0.7-2.8% of GDP) (Muller & Mendelsohn, 2007) . The National Research Council estimated the cost of air pollution to be $120 billion in the U.S. in 2005, a number that primarily reflects health damages from air pollution associated with electricity generation and motor vehicle transportation, largely from adult mortality (Smith, 2005) . Only two analyses of the effects of specific pollutants on child neurodevelopment have been conducted. Grosse et al. calculated the economic benefit of lead reduction in terms of IQ gain and related lifetime earnings for each yearôs U.S. cohort of 3.8 million 2-year-old children to range from $110 billion to $319 billion (base case $213 billion) (Scott D. Grosse, Thomas D. Matte, Joel Schwartz, & Richard J. Jackson, 2002). Trasande et al. estimated the attributable cost of methyl mercury exposure to the developing fetus from American anthropogenic sources of $3.1 billion annually (range from $0.4 to $15.8 billion) (Trasande, et al., 2005).

As illustrated by the case of lead, there are direct and measurable social and economic benefits of environmental policy that accrue to the entire population, not only to the less advantaged groups. The dramatic decline in childhood lead poisoning in the United States represents a major public health success (HHS, 2002) and is credited with reduction of costly delinquency and violent crime. Studies have shown that early exposure to lead is associated both with decreased IQ and antisocial and delinquent behavior that imposes huge economic costs on society (Needleman, Riess, Tobin, Biesecker, & Greenhouse, 1996). The reduction in lead exposure in the 1970s is considered to be an important factor in the significant drop in violent crime in the 1990s (Reyes, 2007). Thus, the regulation of lead under the Clean Air Act, not intended as a social policy, has resulted in an important unanticipated social benefit.

More research is needed on the monetized benefits of reducing pollution, in the overall population and as they affect less advantaged populations. The third paper entitled ñPrenatal Exposure to Airborne Polycyclic Aromatic Hydrocarbons and IQ: Estimated Cost of IQ reductionòaddresses the gap in understanding of the potential economic benefits of reducing environmental pollution and estimates the increase in IQ and related lifetime earnings that would be expected in a low- income urban population as a result of a modest reduction of ambient concentrations of the combustion related pollutants, polycyclic aromatic hydrocarbon (PAH).

The dissertation presents these three interrelated original papers providing new evidence supporting a broad, integrated policy that addresses environmental degradation and inequality. These three papers stand on their own as original contributions to the field. By addressing three important research gaps, they provide needed evidence to support greater protection of children through an integrated social and environmental policy.

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PAPER 1

The Role of Science in Child Labor Reform in the Early Progressive Era (1870-1900)

I. Introduction

Child labor reform in the late 19th century represents a milestone in the translation of science to policy. For the first time, scientific recognition of childrenôs biological and psychological vulnerability in the late 19th century was a major factor in shaping public policy. After that time, the susceptibility of the young was a given, reflected in key events such as the establishment of the American Pediatric Society in 1889, the National Child Labor Committee in 1904, the Childrenôs Bureau in 1912, the ultimate abolishment of child labor in the U.S. in 1938, the passage of the federal óSuperfundôLaw of 1980, and the 1997 Executive Order that ñeach Federal agency shall ensure that its policies, programs, activities, and standards address disproportionate risks to children that result from environmental health risks or safety risksò (EPA, 1997).

The recognition in the late 19th century of the risks of the toxic and stressful environment faced by children in the workplace was a catalyst for the development of the field of childrenôs environmental health, an important branch of public health. The process that led to the New York State Child Labor Law of 1886 is an early example of efforts to put in place a science-based social and environmental policy regarding the protection of childrenôs health and development. Yet the role of science as a force in shaping the perception of the value of the child and as a driver of reform during this period has not been widely recognized.

The public perception of the nature and value of children is the key to understanding how U.S. social and environmental policy concerning children has evolved (Mintz, 2004). The movement to protect child workers in the early progressive period (1870-1900) reflected a dramatic shift in the public perception of the value of children and societyôs responsibility to protect them. Whereas in the pre-modern or colonial period the young had been viewed by all

socio-economic classes as adults in training and as an integral part of the familyõs economic well-being, by the late 19th century middle- and upper-class parents had adopted the ñRomantic idealò of children as innocent and fragile, requiring nourishment of their reason and protection from adult realities (Mintz, 2004). Portraits of children (below) vividly demonstrate the change in how children were viewed between the 17th century when children were regarded as ñlittle adultsò and the latter part of the 19th century when children had become, in Zelizerõs words, ñemotionally pricelessò (Zelizer, 1994).

Most writers have attributed the change in the perception of the value of the child during this period mainly to socio-economic, cultural, and moral factors (Zelizer, 1994). This paper will focus instead on the role of scientific evidence, acting in conjunction with these other factors. It will describe how the growing understanding of physicians, toxicologists, sociologists, and psychologists that childhood was a biologically vulnerable period of life informed progressive reformers who used this knowledge effectively to advocate for change. The intertwining of scientific knowledge with socio- economic and moral factors is illustrated by the collaboration of trained professionals, educated female reformers, society philanthropists, and union leaders in achieving child labor reform.

The paper covers the Early Progressive period from 1870 to the turn of the century, centering on the turbulent events leading to the passage of the 1886 New York State law. The forces leading to the passage of that law reflect the larger social and cultural transformation occurring at the same time in other industrialized states in the U.S., although not in the agricultural states of the South.

The term ñscienceò here refers broadly to knowledge gained by empirical methods, by means of direct and indirect observation or experience. It is not ñmodern science,ò supported as today by molecular biology, workplace monitoring, biomonitoring, and quantitative toxicological and epidemiological data on workplace exposures and dose-response relationships.
Nonetheless, as will be described, by the late 1800s a growing and reliable body of knowledge

had been gathered on the biological vulnerability and the special needs of the child. Although the direct (primary source) accounts of conditions in which children worked are limited in number, those that exist are detailed, well-informed, and rich in detail.

The Mason Children, 1670, Anonymous, oil, American

Kate Rosalie Dodge, 1854, John Wood Dodge, American, Watercolor on ivory, Metropolitan Museum of Art

Not considered here are Eugenics and Social Darwinism, both popular theories in the late 19th and early 20th centuries (Allen, 1989; Leonard, 2005; Piott, 2006). Although some progressive reformers espoused eugenics (the attempt to improve the human species socially through better breeding and environmental nurturance, partly in negative reaction to immigration), most rejected the reasoning of Social Darwinism that society was an organism within which only the fittest, based on innate characteristics, would flourish, and that government should not interfere in this supposedly natural process (Piott, 2006). Unlike progressive reformers who embraced evidence of the vulnerability of the child as a rationale for governmental intervention, believers in Social Darwinism questioned the evidence and opposed child labor reform as an encroachment on liberty by government and a violation of the rule of the family (Piott, 2006).

In the latter part of the 19th century, as now, there was an active interchange between science and cultural values: scientific knowledge and methods used by scientists influenced the way individuals viewed society, while individual and societal values affected the nature of scientific research and interpretation of results (Allchin, 1999; Gould, 1996; Takacs, 1996). For example, although their counterparts in the first two decades of the 20th century were overly influenced by the advances of bacteriologists and the triumph of the germ theory of disease to emphasize agent- specific etiology (Derickson, 1992), reformers and scientists in the late 19th century held the view of the ñwhole childòand considered the breadth of effects of early labor on physical and mental growth, health and development (Derickson, 1992). They also communicated their concern about ñtransmissibleòeffects in succeeding generations.

The reformers were successful in using science to help shape opinion on the social issue of child labor. In this, they were assisted by a cooperative press that facilitated the rapid diffusion of scientific knowledge to the public and among reformers in different states. The effective communication of scientific understanding of the biological and psychological vulnerability of children is illustrated by writings in newspapers, periodicals and reports of the latter 19th century ("The Children at Work," 1886; Congregationalist, 1887; DeGraffenried, 1890; A. P. Stevens, 1894; Woodbridge, 1894). By focusing on the recognition of a biologic basis for the adverse effects of child labor and the translation of that knowledge to a powerful social and political movement, the paper addresses an important gap in research.

II. The 1886 New York State Child Labor Reform Law

A. Narrative of events

In 1886, the New York State Legislature passed legislation to protect child workers (Fairchild, 1905). The history of its passage provides valuable insights into the force of science, along with concern about social justice and economic arguments, in shaping a new child-protective social policy.

The earliest legal restriction on child labor in the U.S. was a Massachusetts law in 1837 which prohibited manufacturing establishments from employing children under age 15 who hadnôt attended school for at least three months in the previous year. Although the New England unions had condemned child labor for endangering childrenôs well-being and health, the focus of that law was the provision of education to children ("Child Labor in U.S. History," 2012). A few other states had adopted similar laws, but legislation enacted before 1880 generally contained only weak restrictions and little provision for enforcement. In the late 19th century, however, social pressure against child labor became more organized. Soon after the passage of the1886 New York State Child Labor Law, Pennsylvania followed suit. By 1899, forty- four states and territories had some type of child labor law (Friedman, 2010).

With the developing market economy in the early 1800s, production had shifted from the home to textile mills and other small industries. By the mid 1800s, the New York City environment had been dramatically altered by industrialization, the influx of immigrants, and spiraling violence (Ashby, 1997; Niederkorn, 1874). In the 1830s and 1840s, 2.5 million immigrants-- almost half Irish Catholicsð had surged into the nation, most into the cities. The slums of New York Cityôs Five Point Section on the Lower East Side became a symbol of a city in crisis. In 1842, Charles Dickens wrote that he found the conditions there among the worst he had ever seen (Ashby, 1997). In 1850, New York City, then only Manhattan and the Bronx, had 300,000 residents (Ashby, 1997). By 1870, the population of New York City had increased, to over a million people, of whom half were foreign born (NYSPCC, 2012). Huge numbers of poor lived in miserable shacks. The mortality rate for children under five was a staggering fifty- two percent (Ashby, 1997). Public and private service systems were overwhelmed, riots and crime

were frequent, and child cruelty and exploitation were common (NYSPCC, 2012). Violence was rampant in New York City as in other urban areas in the U.S. Between 1830-1865, more than 1,000 people died in riots that racked almost three-fourths of American cities (Ashby, 1997). There were increasing fears of an urban crisis with spiraling crime and what was termed õmob rule.ò

Demand for child labor in New York City was high in the mid 1800s, particularly in textiles, canning, mining, and street peddling, where children as young as six or seven worked long shifts. In the 1870s, nearly 100,000 children were employed in factories and shops in New York City and its suburbs ("Children's Rights: the Proposed Factory Law," 1874). Photos by reporter and reformer Jacob Riis (below) showed poor working children of New York City and contrasted dramatically with the seemingly bucolic lives of children of the previous century, many of whom worked on family farms or as apprentices in training for a profession.

By the mid 1850s, the economic and educational discrepancy between rich and poor in New York had grown dramatically. The wealthy mercantile class and the older, established families enjoyed prosperity, educational advantage, and positions of power in sharp contrast to the families of the poor who were largely uneducated and foreign-born. The privileged class in New York, as elsewhere, had a dual view of the problem of child labor: it was both a wrong that needed righting and a threat to their own security.

In 1853, Charles Brace had founded the New York Childrenôs Aid Society. In 1871, the Society presented a bill focusing primarily on child education that prohibited child labor under 10 years of age (and under 12 if the child was unable to read intelligently), with a limitation of 60 hours of labor per week for children under 16, and prohibition of labor under 16 if educational requirements were not met. The proposed bill included the promotion of sanitary conditions and protection from dangerous machinery, but did not bar children from hazardous occupations. The 1871 bill was unsuccessful; but a compulsory, but weak, school law was passed in March 1874 requiring that child workers under 14 must have attended school at least 14 weeks of the previous year (Ashby, 1997). Also in 1874, Elbridge T. Gerry, a prominent New York City lawyer, and Henry Bergh, the son of a wealthy shipbuilder and founder of the Society for the Prevention of Cruelty to Animals in 1866, were moved by the riveting case of 8 year old Mary Ellen Wilson, to form the New York Society for the Prevention of Cruelty to Children.

The case of Mary Ellen Wilson, who had been abused by her caretakers, attracted considerable attention in the press and she quickly became a óposter childô for the vulnerability of the young (Tribune, 1874b). Gerry brought eight year old Mary Ellen to testify in court and requested public custody of the child. Mary Ellen was in rags and had been wrapped in a carriage blanket by a policeman. Her story became a õsocial and cultural lightening rodò, receiving substantial press coverage (Ashby, 1997). It undoubtedly helped that the child was attractive, white and õsurprisingly intelligent.ò Although not herself a working child, she personified the vulnerable child needing special protection. The reporter and photographer

Jacob Riis was present in the court and wrote: ñThe story of little Mary Ellené stirred the soul of a cityé and as I looked, I knew where the first chapter of childrenôs rights was being writtenò(P. Stevens & Eide, 1990). When, outside the courthouse, Etta Wheeler, a Methodist social worker and reformer, asked Bergh if it was time for an anticruelty society to protect children, he agreed. One year later, Gerry and Bergh founded the New York Society for the Prevention of Cruelty to Children, assembling a board of influential and affluent men, who like them, were well educated, strongly conservative, moved by the Mary Ellen story, and also concerned about the impending urban crisis (Ashby, 1997). Moreover, Mary Ellenôs persecutors had an Irish name, ñConnollyò; Gerry and Bergh probably knew that highlighting cruelty by immigrants or people of recent immigrant descent would get the attention of Yankee donors and legislators. The stated purpose of the New York Society for the Prevention of Cruelty to Children was "to rescue little children from the cruelty and demoralization which neglect, abandonment and improper treatment engenderò(NYSPCC, 2012).

In 1882, a bill was drawn up by Gerry, then President of the New York Society for the Prevention of Cruelty to Children and Dr. Abraham Jacobi, then President of the New York State Medical Society, that provided that no child under 14 could be employed unless a physician certified that the child was healthy; no child over 14 could be employed for more than 10 hours a day or in certain specified hazardous industries (including mining, glass work, mercury, lead, arsenic, iron or brick works, tobacco products, or manufacturing in living quarters); and no child under 14 years could be employed in occupations involving the use of dangerous machinery. It seemed probable the bill would have passed the Assembly except that the session closed before it was brought to a vote (AEA, 1890).

In 1883, the New York Society for the Prevention of Cruelty to Children renewed its effort; but the factory interests of the state, which had been ñcaught nappingòthe previous year, loudly opposed the factory bill and it was defeated (AEA, 1890). Later in 1883, at the request of Gerry, the Children in Factories Bill was proposed by then New York State Senator Thomas F.

Grady. The proposed bill prohibited the employment of any child under the age of fourteen by any manufacturing corporation within the State, unless on the certificate of a physician as to his/her physical condition; and it limited the employment of children over 14 (Tribune, 1874a). Senator Grady argued that the employment of children under the ages mentioned was deleterious to both health and morals. It was not only an injury to the children, but also to the adults who were deprived of work by reason of the large employment of children. Senator H. A. Nelson, a successful Irish immigrant, denounced the bill, citing instances in his native county of Ulster, Ireland, where thousands of children under the ages mentioned in the bill were ñhappily and healthfully employedòand were the means in many cases of supporting themselves and their parents. Although the bill was opposed by immigrants who relied on the wages of their children, this group lacked political power to block the bill. Moreover, the bill had strong support from a newly powerful source--organized labor--that increasingly feared competition from the growing, low-cost workforce of children (Mintz, 2004). Nonetheless, the 1883 bill did not pass.

In 1884, the Workingmenôs Assembly joined forces with Gerry and the New York Society for the Prevention of Cruelty to Children to produce a new bill. The new bill was more stringent than the proposed 1882 bill, requiring an affidavit stating age and place of birth for children between 14 and 18; requiring a physicianôs certificate for children under 18; barring employment at dangerous machinery or in certain specified occupations (as in the proposed bill of 1882) or in any place not properly lighted and ventilated; and limiting work hours to 10 per day or 60 per week for children under 21. Enforcement was put in the hands of a factory inspector. Gerryôs bill passed the Senate; but on its final passage in the Assembly was denounced as ñtoo radicalò

At this critical juncture, organized workingmen played a key role in supplying data on the extent of child labor. They received material assistance from the State Bureau of Labor Statistics which issued a report in January 1885 on the extent and conditions of employment of young children in factories of New York State. The Bureau undertook its study in response to a resolution of the State Trades Assembly passed in January, 1884 (AEA, 1890). A contemporary

article noted that ñThis work must be placed to the credit of the organized workers of New York State, since the Bureau of Labor Statistics was to a certain degree their official mouthpieceò (AEA, 1890).

Again in 1885, bills were introduced jointly by the New York Society for the Prevention of Cruelty to Children and the Workingmenôs Assembly. Aware of the growing demand for reform of child factory labor, the growing political power of the Workingmenôs Assembly, and the powerful cooperation between the New York Society for the Prevention of Cruelty to Children and the Workingmenôs Assembly, New Yorkôs Governor David B. Hill wrote to Gerry for his advice. Hill then presented Gerryôs views in a message to the legislature strongly urging regulation of child labor in factories (AEA, 1890). In 1886, the bill drafted by Gerry and again jointly supported by the New York State Society for the Prevention of Cruelty to Children and the Workingmenôs Assembly was introduced and a bill was finally passed. The law as passed differed in many important respects from the bill first advocated, ña number of points being yielded to its opponentsò(Fairchild, 1905). These included the lowering of the age limit for the employment of children from fourteen to thirteen years and the omission of the ban on employment of children under sixteen in the use of dangerous machinery or in specified occupations. Nevertheless, the New York Child Labor or ñFactory Actòof 1886 was the first meaningful attempt to protect children working in factories (Felt, 1965). Before its enactment in 1886, child labor in the factories of the most populated state in the union was practically unregulated. ñThe real problem of factory legislation, the hours of labor of women and children, the prohibition of child labor under a certain age, with proper restrictions, educational and otherwise, above that age, the sanitary and moral conditions of factory employment, the safe-guarding of life by guarding machinery and elevators and requiring fire escapes; these and other subjects of like nature had not been touched by the legislation of the stateò(Fairchild, 1905).

The series of events described here ended in a significant action that was an important step in protection of children (P. Stevens & Eide, 1990) that was followed by increasingly protective legislation. Passage of the New York State Child Labor Law of 1886 was a complex and dynamic process. Many factors were involved; each is discussed below.

B. Science

Status of the sciences in the late 19th century:

The focus of this paper is on the recognition by reformers of the biological and psychological vulnerability of the child that reflected their growing understanding of the science of toxicology and child development. They were also informed by advances in the emerging fields of pediatrics, sociology, and psychology, occupational and environmental epidemiology during the latter 19th century. However, a detailed account of each field is outside the scope of this paper.

By the 1880s, the sciences had expanded dramatically, reaching and engaging a popular audience, and influencing the way people viewed the world (Fyfe & Lightman, 2007). There was wide public awareness of the theory of evolution and the evidence that natural processes were guided by universal laws. The industrial revolution with its technological advances, often with direct practical benefits to society, had stimulated scientific inquiry in biology and medicine, physics, and chemistry. This was a time of public optimism about the role of science in human progress.

Between 1865 and 1900 the recognition of childhood as a special and vulnerable period of development led to the formal establishment of academic societies and associations focusing on children in the fields of medicine, sociology, and psychology. A new medical field and specialized institutions were created to treat childhood diseases and preserve the health of

children (Zelizer, 1994). In 1880, the American Medical Association organized a pediatric section, which became the foundation for the American Pediatric Society, established in 1889. During the late 19th century, universities created their first departments and programs for the newer ñscientificò social sciences of sociology and social psychology (Krieger, 2000; Ross, 1979). In 1865, the American Social Science Association was founded, providing, among other things, an institutional setting where women were able to undertake empirical research (Smuts, 2006). In the 1890s, Emile Durkheim established the field of academic sociology with an emphasis on social research (Durkheim, 1895).

The American Psychological Association was founded in 1892 by G. Stanley Hall, an American psychologist at Clark University who found a theoretical framework in Darwinian evolutionary theory and pioneered the Child Study Movement in the U.S. in the 1880s. Hall espoused the late 19th century Romantic view of childhood and proposed that knowledge emerging from the scientific study of children should be used to liberate the natural, uncorrupted child (Smuts, 2006). A strong believer in the scientific method, his empirical research on child development not only demonstrated that children were psychologically distinct from adults but that they also underwent distinct stages of development --infancy, childhood, adolescence (Smuts, 2006; Zelizer, 1994). Smuts has described the impact of Stanley Hallôs belief that knowledge emerging from the scientific study of children should be used for social progress--to transform all institutions affecting children (Smuts, 2006). Working with Arnold Gesell, Hall collected a large body of data on the growth and development of the child from infancy through adolescence. Their normative data became the standard for parents, teachers and pediatricians in evaluating childrenôs development. The research of the Child Study Movement reinforced the importance of the early childhood years and of the importance of early childhood programs (New & Cochran, 2007).

Additionally, the evolutionary theories of Charles Darwin, as historian Linda Gordon has noted, ñdecreased the felt distance between humans and animalsò(Ashby, 1997). In response, new standards of refinement and respectability were adopted ñto separate humans from animals . . . . While we may have been descended from the ape, we were civilized and moral beingsò (Ashby, 1997). The discovery in 1849 that anesthesia could treat pain also contributed to the notion that suffering was not inevitable (Ashby, 1997). Darwin himself provided a scientific model by studying his own children and recording their cognitive and emotional development (Smuts, 2006).

In the latter 19th century, the sciences of occupational and environmental epidemiology were in an early stage. One of the first occupational epidemiological studies of risks to children had been that of Sir Percival Pott who in 1775 reported an association between exposure to soot and a high incidence of scrotal cancer in young English chimney sweeps (Gordon, 1993). However, occupational and environmental epidemiology did not become quantitative disciplines until the 20th century (Stellman, 2003).

During this period, industrial toxicology also was not yet a formally established field. Rather it mainly took the form of detailed observations by factory inspectors, statistics from surveys, and in-depth reports by health and labor professionals. The very first essay in the U.S. on the diseases of work, written by Dr. Benjamin McCready and entitled ñOn the Influence of Trades, Professions, and Occupations in the United States in the Production of Diseaseò, had been published in 1837, warning against child labor, long hours, and poor ventilation (Felton, 1976; McCready, 1837). However, it was not until 1914 that the U.S. Public Health Service Office of Industrial Hygiene and Sanitation and the Conference Board of Physicians in Industrial Practice in the Eastern States were established. The first American text on industrial toxicology by Dr. Alice Hamilton, Industrial Poisons in the United States, was not published until 1929. Nonetheless, many articles, reports of surveys, and descriptions of working conditions and industrial disease began to appear in the second half of the 19th century (Felton, 1976). These

included state investigations of workplace conditions and publication of the results by State Bureaus of Labor Statistics. These Bureaus were organized in ten states between 1869 and 1883, producing and distributing data on child workers (Zelizer, 1994). Massachusetts had set up the first such bureau in 1869; New York had followed in 1883. The Bureaus conducted investigations into all facets of labor and industry and published the data in their annual reports. The investigators sent questionnaires to employers, interviewed workers, collected descriptive and statistical data on deaths, injuries and illnesses, and investigated unhealthy trades. Their published reports constituted a detailed account of the hazardous conditions under which over a million American children worked. In 1884, after two decades of advocacy by the unions and state commissioners of labor statistics, a permanent, the Federal Bureau of Labor Statistics was established to collect and analyze information about employment and labor, and disseminate essential statistical data to the public, Congress, other Federal agencies, and State and local governments. The Bureau's early investigations ranged widely over economic and social developments in the United States and were directed at social issues concerning laboring women and children (Goldberg & Moye, 1985). In 1870, for the first time, the U.S. Census provided a separate count of adult and child workers. This published information reached the public through the work of reformer-writers and a sympathetic press, providing a powerful argument for reform. Thus, the rise of state bureaucracy and the competence of the state was an important factor in child labor reform.

Understanding of the biological vulnerability of the child and the risks of child labor:

By the last decades of the 19th century, the public had become aware that children were biologically vulnerable, differing from adults in their biologic response to toxic exposures and psychosocial stress. As highly educated people, philanthropists such as Elbridge Gerry,

reformers such as Etta Wheeler, physicians such as Dr. Abraham Jacobi, and politicians such as Thomas Grady were well informed of the evidence of the susceptibility of the young. As these reformers were members of the high-status class, the photographs by Jacob Riis of poor urban children would have aroused their passion over protecting children from harm and exploitation in the workplace (Mintz, 2004). At the Annual Meeting of the Medical Society of the State of New York in 1882, Dr. Jacobi, then President of the Society, ñaddressed attention to the want of legislation to protect factory children in New York Stateò. He recommended that children employed in factories should be under official supervision; before being admitted to factory work a child of legal age ought to undergo a medical examination; cholorotic, anaemic, scrofulous, crippled, scoliatic, bronchitic, and phthisical children, and those under the normal size for their age should be excluded; no night or Sunday work ought to be permitted; some branches of work should be forbidden entirely such as mining, glassworks, rag-sorting, factories using mercury, lead, arsenic, etc., and in match factories; and the earliest age at which the young ought to be admitted to manufacturing employments ought to be fourteen years. ñUp to the period of puberty the energies of life and mind needed in the development of individual should not be wasted recklesslyò("Telegraph from our Special Reporter," 1882).

Professionals and reformers (often the same people) writing at the time were knowledgeable about the toxicity of the working environment and the special susceptibility of the young during critical life-stages. In addition, as we will see, they were able to effectively marshal scientific and observational data to support their arguments for the protection of this vulnerable population. Together, their writings provide a riveting account of the chemical and physical threats to the more than 1,118,258 vulnerable, wage-earning children in the U.S. (A. P. Stevens, 1894). For example, in ñThe Children at Workò(1886), the anonymous author referred to the documentation by Mr. John Swinton of lead- poisoned ñwork-childrenòof New York City and proceeded to describe her/his own personal observation of children in the cotton manufactories:

> é [They] work 65 hours a week for the sum of two and a half cents an houré . For twelve hours they are swallowed up in the roar, dirt, jar, and general hideousness of spinning roomsé [where] the air is composed in equal parts of cotton, tallow, machine-oil, and human expirations, heated to a temperature of seventy-five degreesé .The oil from the flying machinery falls like fountain-spray through the room. It saturates the clothing and plugs every pore of the body with aid of the cotton-dust. The machinery is heavy, armed with dangerous gearing, belting and pulleysé . First joints of little fingers often disappear in the cruel irons, a whole finger sometimes, at long intervals, a hand or an armé . Hard labor, long hours, bad air, bodily risk, and moral death are the demons to whom the children are handed over for the sum of one dollar and a half a week. ("The Children at Work," 1886)

Alzina Parsons Stevens, an assistant factory inspector in Illinois, wrote about the health risk to these young textile workers, concluding that ñin textile manufacture, the dangerous machinery, contaminated atmosphere, and inhumanely long hours do not permit normal development of a growing childò(A. P. Stevens, 1894).

Knowledge of the risks of physical injury and chemical poisoning in the workplace is evidenced by many other writers in the popular press. In 1873, an article in *Harpers New Monthly Magazine* noted that over 100,000 children were at work in the factories of New York City and the neighboring districts, with another 15,000-20,000 who are ñfloatersòdrifting from one factory to another. Describing in detail the work environments of envelope factories (8,000 children), gold-leaf factories (number unknown), artificial flowers (10,000-12,000 children), and tobacco manufactories (10,000 children), the writer concluded that tobacco manufactories have ñby far the most noxious environment in which the under-ground life in these damp caverns tends to keep the little workers stunted in body and mindò("The Little Laborers of New York City," 1873).

Clare DeGraffenried, a graduate of Wesleyan College in 1865 and an investigator with the U.S. Bureau of Labor assigned to research the condition of wage-earning women and children (Whites, 1988) was one of the first labor investigators in the U.S. She published twenty-seven articles regarding the labor movement and won awards for essays on child labor and

working women (Scott, 1984). DeGraffenreid painstakingly detailed the many adverse effects of tobacco poison: ñextreme nervousness, maladies like St. Vitus Dance, physical weakness, disordered digestion, heart action impaired, strength sapped; the mind is excited, often the passions are inflamed and the moral sense deadenedò (DeGraffenried, 1890). Alzina Parsons Stevens also observed these ills firsthand:

> To know how a child is affected who breathes this atmosphere all day, bent over a tobacco bench, take up her hand and examine the shrunken, yellow finger tips, the leaden nails; lift her eyelid, and see the inflammation there; examine the glands of her neck, her skin; lay your hand upon her heart and note its murmur. Nor does the injury to the girl child in the cigar factory end with herself. The records of the medical profession show that women who have worked in the tobacco trade as children are generally sterile. When their children are not stillborn, they are almost invariably puny, anemic, of tuberculous tendency, the ready prey of disease. (A. P. Stevens, 1894)

De Graffenreid made similar points about the special risks to children:

> Further, in employments making tinware, buttons, frames for umbrellas or satchels, almost every worker has the end or joint of a finger cut off or the whole hand mutilated. In type foundries and toy manufactories, the danger is lead poisoning (DeGraffenried, 1890). The twine factories (numbers unknown) have dangerous machinery capable of removing fingers or limbs. The air is filled with floating particles of cotton and flax and must be ñexceedingly unhealthfulò ("The Little Laborers of New York City," 1873)

DeGraffenreid described how the glass industry wrecks the health of boys while frame gilding stiffens the childôs fingers; work in a tailor or sweat shop produces spinal curvature, and for girls ñother diseases which mean lifelong pain and loss of power to bear healthy childrenò; in bakeries, children roast before the ovens; in binderies, paper-box, and paint factories they are exposed to arsenicals, rotten paste and poisons of paints; in metal factories the dust produces lung disease, there are accidents with hot metal, and deafness is produced by the hammering of plate (A. P. Stevens, 1894). In addition to diseases incidental to the trades, the conditions of bad sanitation and long hours threaten childrenôs health and development (DeGraffenried, 1890).

These writers underscored another threat as insidious as the physical toxicants: the psychological harm and moral degeneration resulting from exhausting labor, scanty food, and lack of education. Alice L. Woodbridge, Secretary of the New York Working Womenôs Society, wrote:

> With mind and body exercised beyond the natural limits, it is impossible for [children] to appreciate the innocent pleasures of childhood; they become the victims of abnormal appetites and desires and moral degeneration naturally follows. This is proven by the fact that seventy per cent of the children in reformatories are the offspring of working people. (Woodbridge, 1894)

Underpinning this detailed enumeration of the physical and psychological threats to child health and development was an evolving understanding of the biological susceptibility of the young:

> The period from seven to fourteen is the most vital in the growth of the childé . [M]any children are engaged at tasks too great for their physical strength, becoming consumptive in consequence or suffering serious bodily harmé . These years when mind and body are susceptible of the healthiest growth are spent in a monotonous round of indoor drudgery which undermines the constitution, stunts the intellect, debases the higher natureé . (DeGraffenried, 1890)

Because of concern for future generations, many reformers placed great emphasis on risks to girls between 14-16 years of age:

> [This is the] most dangerous interval in the development of womanhood; when as all physicians, educators and students of social science testify, the establishment of those sexual functions essential for the perpetuation of the race must not be imperiled by any undue strain on mind or bodyé . [S]ince the physical organization of the female is of greater delicacy and more easily affected by unfavorable environment, the stronger is the likelihood that the shattered constitution of the girl-worker will bequeath to generations yet unborn the scourge of inherited blood poison and the moral curse of racial depravityé . (DeGraffenried, 1890)

Not only did science help to shape the perception of childhood but, while before the late 19th century social reformers had relied mainly on moral admonition, progressive reformers after 1870 believed in scientific research as the instrument for reform. The writings of social reformers prior to this period did not evidence much awareness of the biological and psychological susceptibility of the child. Their main preoccupation was with childrenôs need for schooling, amusement and exercise. Between the 1830s and 1870, reformers concerned with the well-being of children, and child workers in particular, primarily stressed the need for their education as an antidote to immorality and crime (Landon, 1838). They emphasized the practical need to educate child workers in the shortest amount of time:

> The children who frequent our Public Schools are the offspring of those who are in indigent circumstances. Time to them is money. Their childrenôs labor, at the age of twelve or fourteen years, becomes an object of importance,--absolutely essential to procuring the necessities of life. At that age, they must consequently be removed from their scholastic duties. If such be the circumstances of those who seek public instruction as the only mode of educating their youth, it becomes necessary that the greatest amount of information should be conveyed in the shortest time. ("Public Schools in New-York," 1835)

In 1838, discussion of the legislation in Connecticut, Massachusetts and Rhode Island regarding the education and employment of children in factories made no mention of physical or psychological harm of child labor ("Legal Provision Respecting the Education and Employment of Children in Factories," 1842). These laws stipulated that children were ineligible to be employed in factories unless they had received at least three months of schooling out of the twelve months in the year preceding employment.

In 1843, Blanchard Fosgate, M.D., a member of the New York State Medical Society, noted that poor health of child laborers is attributed to long working hours, continued confinement, and lack of exercise and again stressed the need for education:

> Many children enter factories at the early age of from six to twelve years, just when the rudiments of an education should be instituted, to prepare them for after-usefulness; and when the animal organization is being developed with more rapidity, and liable to greater injury from diliterious [sic] influences, than during the more advanced stages of life. . . . Fortunately, the remedy for the evil is as clearly perceived as its necessity, and is as clearly within our application. The cure consists, in properly directed universal education. When the laws are so framed, that the common school shall furnish daily employment to every child during that period of life now contemplated by its benevolence, the first step in the great reformation will be accomplished. (Fosgate, 1843)

In 1847, Horace Mann, then Secretary of the Massachusetts Board of Education, laid down the õpostulate that every child of the human family has the same right to an education that he has to inhale the air which keeps him in life, or to enjoy the light of the sun, or to receive that shelter, protection, and nourishment, which are necessary to the continuance of his bodily existenceò("Horace Mann: Analysis of Mr. Mann's Reports as Secretary of the Massachusetts Board of Education.," 1858).

Reformers also focused on the need for amusements and sports for young workers:

> Let a careful observer visit the manufacturing establishments where children are employed at an early age, and for as many hours per day as the adult is engaged, and he will find suffering, that results in disease, and premature old age or early death. Here, the child has no time for recreation or amusement; with him it is work, work, work! And he thus works on through his miserable existence, and dies without having lived through half his days. (Bulkley, 1859)

C. Socioeconomic factors

The social and economic transformation wrought by the industrial revolution and the massive influx of immigrants to the Eastern Seabord States were the root causes of the surge in child labor in the U.S. and New York City in particular. The transformation also created new forces that led to reform of child labor law but made the process a highly contentious one, with factions split along socio-economic lines. Ironically, ñthe very period that freed middle class children from work and allowed them to devote their childhood years to education also made the labor of poorer children more essential to their familiesôwell-being than in the past, and greatly increased the exploitation that these children sufferedò(Mintz, 2004). Poor immigrant parents believed that their offspring had an obligation to contribute to their householdôs well-being (Ashby, 1997; Mintz, 2004; Zelizer, 1994). In fact, most immigrant families depended on their childrenôs labor, whether for childcare, shopping, cooking, scavenging in the streets, or paid work inside or outside the home. Therefore, they opposed child labor laws. As noted above, while privileged people viewed children as being in need of protection, they also saw poor children (especially children of immigrants) as a potential threat to society. In fact, by the 1870s they were deeply anxious about escalating labor unrest and urban disorder and attributed these trends to the surge in immigration (Ashby, 1997). An editorial on child labor in a widely read magazine voiced the worry: ñThe employment of children of tender years has two evil results. It deprives them of the opportunity of education, and it stunts their physical development. They often grow up sullen, and with an undefined sense of being wronged. The dangerous classes are apt to increase in this wayò(Congregationalist, 1887).

Social and economic changes in the latter 19th century led to the rise of new players: educated women, newly empowered labor unions, and philanthropists and charitable organizations actively engaging in public policy. By the late 19th century, many American women had received higher education (Harwarth, Maline, & DeBra, 2006). In 1870, an estimated one-fifth of resident college and university students in the U.S. were women; by 1900 the proportion

had risen to over one third (WIC, 1994, 1995). Here was a new social phenomenon: women who for the first time were educated but had few opportunities for jobs other than teaching and therefore devoted themselves to social causes. Although their ranks included professional women like Stevens, DeGraffenried and Woodbridge, most college- and university- educated women were not themselves trained scientists (Rossiter has written about the systematic failure to recognize the role of those women who did enter the sciences (Rossiter, 1982, 2002)). However, many educated women not only understood the new science about childrenôs susceptibility to environmental and social stressors but also recognized the substantial social and economic costs of child labor.

Teaming up with scientists, educated women became the leaders, the innovators, and a driving force behind the new sciences of childhood and their application to reform. The chief aim of social feminism during the Progressive Era in the U.S. was to promote and protect the welfare of women and children (Smuts, 2006). Moving far beyond early efforts such as the Fresh Air and Exercise Movement to become a national political force, these reformers eventually succeeded in 1912 in founding the Childrenôs Bureau, the first governmental agency in the world created solely to consider the problems of children (Smuts, 2006). However, it was the cause of child labor that most energized the reformers from the latter 19th century until 1938 when the Fair Labor Standards Act prohibited most employment of minors.

In ñThe Children at Workò(1886), the writer (anonymous but probably a woman) states:

> It is with women chiefly that the future rests. It is women who, more and more, are searching out causes and seeking to discover what method may best alter certain social tendencies and evilsé [A] united demand that child labor be abolished now and forever would at least open eyes and pave the way for the legislation that is sure to comeé . ("The Children at Work," 1886)

The number of local labor union organizations had increased steadily during the mid 19th century. The National Labor Union (a federation of local unions) was formed in 1866 and was superseded by the American Federation of Labor (AFL) in 1886. In 1880, about 2 per 100 non-agricultural workers were union members; by 1900 that number was almost 5 per 100 (Friedman, 2010). *As early as 1832, t*he New England Association of Farmers, Mechanics and Other Workingmen had condemned child labor. But it was not until 1883 that the New York labor movement led by Samuel Gompers, President of the AFL, successfully sponsored legislation prohibiting cigar making in tenements, where thousands of young children worked in the trade. The power of the unions grew steadily over the last decades of the 19th century. Organized labor supported child labor reform out of concern for childrenôs health and well-being and, even more, fear of competition from this huge low-cost and unorganized workforce. As we saw in the case of the 1886 New York State Law, unions were key partners in securing reform.

In the latter part of the 19th century, charity organizations became the dominant force in American philanthropy (Smuts, 2006). The 19th century saw the proliferation of private charitable organizations like the New York Childrenôs Aid Society founded in 1853 at a time when orphan asylums and almshouses were the only "social services" available for poor and homeless children. As mentioned, this was followed by the establishment of the New York Society for the Prevention of Cruelty to Children in 1875 that played a leading role in the 1886 New York State Child Labor Law.

As did Gerry and other leaders of society, reformer-writers underscored the present and future dangers to a democratic and civilized society: ñThe evil in New York is evidently enormous, and most threatening to our future. These children, stunted in body and mind, are growing up to be our voters and legislators. There are already 60,000 persons in New York who cannot read or write. These little overworked operatives will swell this ignorant throngò("The Little Laborers of New York City," 1873). Moreover, warned DeGraffenreid: ñThe children who persist despite hideous tenement-house influences and congenital weakness are a shambling,

crooked-bodied, narrow-chested, often scrofulous race, physically morbid, morally misguided, craving stimulants and predisposed to crimeò(DeGraffenried, 1890). Of utmost concern, the family structure which was seen by many social workers and reformers as critical to a civilized and functioning society was undermined (Agnew, 2004).

DeGraffenried stated the principle that the ñmoral and physical well-being of the community demands restriction within reasonable limits of the labor of women and children.ò She cited the English factory reform movement from 1802-1878 as the model for the civilized world, resulting in the ñrapid development of the general intelligence of the laboring class, rise of wages, diminution of pauperism and crimeò(DeGraffenried, 1890). She noted that in 1878, the frequency of convictions for crime was 1 in 900 in the U.S. as compared with 1 in 1,880 in Great Britain. In 1885, it had fallen to 1 in 3,272 in Great Britain but remained 1 in 930 in the U.S. As DeGraffenried put it, child labor is a ñsocial and economic wrongé which strikes at the safety of the home, the family, the future manhood and womanhood of the republic.òIn driving home the message that child labor was destructive of the family structure and the role of the father, she cited the census of 1880, which showed a 58% increase in child workers compared with only a 24% increase in adult workers: ñYoung children, and girls oftener than boys, are crowded at low wages into pursuits formerly the resource and mainstay of adult (male) laborers.òThe results: ñThe father is deposed from his rightful position in the family circleé .The sanctity of the family order is destroyed. All bonds are loosed. Authority is a dead letter, respect and reverence for age disappear, the home has no hold on its member.ò

The failure to integrate and educate children of immigrant families was seen as the greatest danger--not only a moral wrong but a threat to the future of society. Stevens presents meticulous data on forty-six children from factories in Illinois, noting that most were foreign-born and few could speak English or knew their letters: ñWe cannot compile such records as theseé and feel confident that we can have óan American cityôin short orderé ò(A. P. Stevens, 1894). She concludes: ñThe prosperity of all nations lies in the development of the working classes.

Humanity is never independenté [I]t is necessary for the general welfare that all classes shall attain the highest state of civilization possible.ò

In 1894, Alice L. Woodbridge, Secretary of the New York Working Womenôs Society, characterized child labor as an obstacle to economic progress (Woodbridge, 1894). She cited the facts that child labor had led to lower wages, generally longer hours of labor, and inferior quantity and quality of production in the industries in which children are employed. In addition, the working classes are the ñpurchasing classesòand employment of children lessened the opportunities of employment of adults and ñthe consumptive powers of the communityò She provided detailed statistics supporting her argument that the employment of children reduced rather than increased family income. Lambasting the present laws regarding the labor and education of children as utterly inadequate and urging further legislation, she concluded: ñLife is worth more than meat, and character than money bags.ò

The anonymous author of ñThe Children at Workò(1886) identified the great corporations that are the sole beneficiaries of the practice as ñone of the two forces that are the giants holding children in a worse than penal servitude.òThe second force is the ñgreedy and indifferent parents or parents stung by necessity with permitting the evil.òThese economic forces set up a vicious circle in which the children were ill-paid, which made their employment at a young age quite necessary; and the father was ill-paid or not employed at all, which forced him to seek the aid of the children. ñThus, the capitalist alone derives any benefit from their debasement.òThe writer then couched moral outrage in economic terms: ñThe bodies and souls, the time, the labor, the youth, the innocence of children have a market value of one dollar and a half in the United Statesò("The Children at Work," 1886).

D. Moral Factors

Contemporary periodicals provide understanding of the mindset and role of the reformer-writers in shifting public opinion away from the acceptance of the moral wrong of child labor. They argued that the practice of child labor was an evil not tolerable in a civilized society. They used every weapon of biblical rhetoric, irony, and fear--conjuring images of Herod, of upper class children rosy in sleep while skeletal, poor children dragged themselves home from work. They predicted a future of an ignorant and illiterate citizenry, physically and morally degenerate as a result of the toxic and corrupting environment in which they were forced to spend half of their ñunnatural lives.ò

The notion of responsibility to protect oneôs needy brethren was part of Americaôs founding history (Winthrop, 1630). However, in the 17th century it was linked with the belief in the inevitability and even the value of suffering. By 1850, many churches had shifted from a theology of suffering to one of a benevolent God (Ashby, 1997). Evangelists emphasized religion of the heart, evoking moral sympathy, with the result that there was increased sympathy for the poor and afflicted. The abolitionist movement, leading to the Civil War and ultimately the 13th Amendment abolishing slavery, further reduced the national tolerance for cruelty and suffering. Therefore, by the 1870s and 1880s, the prevailing moral and religious principles supported interventions to protect children.

Reformer-writers of the late 1800s, mostly women, advanced the moral issue as a primary argument for social change. Child labor was ñan evil which cries out strongly for instant and thorough suppression. How great it is, what havoc it has made and makes among the numerous poor, what ravages of disease and suffering it has inflicted on them, is not known even to the benevolent societies which seek the welfare of the childrenò (DeGraffenried, 1890). The evil had many causes; but reformer DeGraffenried decried the evil of indifference to the suffering of children:

> The citizens of those cities where it is most rife, the Christian superintendents of the concerns which most favor it, the parents who permit it, the clergy who might do much towards its final stamping-out, are hardly aware of its real extent and dreadful results; for the children are patient and ignorant of their own evil condition, and the results are so slow in arriving, so secret in manifesting themselves, that glib argument can trace them to other causes than hard work and long confinement in tender childhood. And glib argument is doing this every day. Custom has staled the consciences of the authorities and sealed the lips of those who are bound to speak. ("The Children at Work," 1886)

The reformer-writers combined high moral principles with a practical optimism. Their credo was ñNo evil is hopeless when its extent is known and its corrective is rigidly appliedé . Though here and there the horizon be dark, the outlook is not discouragingò(DeGraffenried, 1890).

Nor were they afraid to tweak the conscience of the privileged class. DeGraffenried exhorted:

> Think of it, parents, who kiss your pampered darlings of nine and ten years in rosy slumber tucked away at 8 oôclock in the soft, warm bed after a day of romp, wholesome food and wisely managed study! On Sunday mornings the writer has seen at their homes scores of cash-girls and boys heavy-eyed, listless, dragging their tired limbs or asleep in the stupor of exhaustion. Where are the graces, the joys, the innocence of childhood? (DeGraffenried, 1890)

Stevens echoed this theme with superb irony: ñThe children of the so-called upper classes are far better able to perform labor than the children of the pooré the [latter] need larger opportunities for development than the children of the more fortunate classesò(A. P. Stevens, 1894).

DeGraffenried also chided legislators for their moral failure. Noting that two years ago a bill prohibiting the employment of children less than ten years old failed to pass in Georgia, she described the scene in a nearby factory:

> [W]ithin fifteen minutes walk of the capitol, in two large cotton mills, delved fully one hundred pale, dwarfed, goblin-like, infantile creatures, without a ray of learning and every gleam of intelligence fast being extinguished by drudgery--children trebly weakened by descent from mothers and grandmothers whose strength and youth were ground out by the same remorseless machinery in a life-time of similar toil. (DeGraffenried, 1890)

Characterizing child labor as child slavery with indignant references to the Bible, Stevens wrote: ñTo force a child whose only inheritance is a weak constitution into employments which require the fullest development of mind and body is an act which out-Herods Herodò(A. P. Stevens, 1894). She concluded: ñPublic opinion will sometime [judge] that a nation that suffers child labor is unchristian and uncivilized, its code of laws inhuman, its people without moral sense or moral courage.ò

III. Coda and Conclusion

Although the work of child labor reformers in the early progressive era achieved only partial success in regulating the conditions of child labor, by the late 19th century science had clearly emerged as a player in policy-making. True, the abolishment of child labor did not occur until 1938. Moreover, the efforts in New York State resulted in a bill that was far weaker than that proposed. However, it was the first enforceable law in New York State and was followed by

similar legislation in other states. In the long term, science was to have an increasingly powerful effect.

The National Child Labor Committee, an organization dedicated to the abolition of all child labor, was formed in 1904. It managed to pass one law, which was struck down by the Supreme Court two years later for violating a child's right to contract his work ("International Initiative to End Child Labor: US Legislation," 2012). In 1924, Congress attempted to pass a constitutional amendment that would authorize a national child labor law. This measure was blocked, and the bill was eventually dropped. Child labor ended during the Great Depression when adults were willing to work for the same wages as children. In 1938, President Franklin D. Roosevelt signed the Fair Labor Standards Act (FLSA), which placed strict limits on child labor (Smith, 2005). However, in developing countries, threats to childrenôs health from toxic chemicals and unsafe conditions in the workplace remain a serious problem. Today there are more than 250 million economically active children between the ages of 5 and 14 years old, almost half of whom are engaged in hazardous work (Fassa, 2003). Globally more than a million children younger than five years die each year from environmentally-related conditions (Witherspoon, 2009).

The recognition in the latter 19th century of the risks to children in the workplace was a catalyst for the development of the field of childrenôs environmental health. By the mid-20th century, the end of child labor and the public health successes in the reduction of infant mortality and infectious diseases of children permitted a greater emphasis on non-communicable chronic diseases. Today, public health is grappling with the problems of increasing prevalence of childhood diseases that are, in part, environmentally related, such as asthma and developmental disorders. These conditions are now understood to be related to environmental and social factors and, less importantly, to genetics.

A major concern in the U.S is not the dangers to children in the workplace, but the threat from the many toxic chemicals in the environment including air pollutants, pesticides, and chemicals in plastics (CDC, 2009). During the past decade, these contaminants have been routinely found in bodies of pregnant women, newborns and children (CDC, 2009). There has been an exponential growth in scientific knowledge during the past several decades, about the mechanisms involved in the biological vulnerability of the developing fetus, infant and child both to the toxic effects of environmental pollutants and to psychosocial stressors associated with poverty or race/ethnicity (Anderson, Diwan, Fear, & Roman, 2000; Grandjean & Landrigan, 2006; National Research Council, 1993; F. Perera & Herbstman, 2011; F. P. Perera et al., 2004; World Health Organization, 1986). This knowledge has led reformers of the 21st century to call for new legislation to protect children from toxic chemicals in the environment. In addition, the socio-economic and racial disparities in the well-being of children have become more pronounced, leading to an ever-stronger environmental justice movement centered around children (Landrigan, Rauh, & Galvez, 2010).

The final decades of the twentieth century witnessed remarkable progress in advancing children's rights and well-being worldwide, including the 1989 Convention on the Rights of the Child that became the most widely adopted human rights proposal in history (Bauer & Boyce, 2004). Despite this great promise, adverse psychosocial, economic, and environmental conditions are commonplace worldwide, affecting the health, well-being, and prosperity of individuals and societies. Effects of childhood adversity persist over a lifetime and thus have implications for society as a whole. ñChildren may thus represent a demographic ôkeyô capable of unlocking the science and knowledge of human behavior and health in addition to representing a treasured presence within the human populations of the worldò (Bauer & Boyce, 2004).

As the work of protecting children continues into the 21st century, scientific evidence has become increasingly important as a driver of policy, not alone, but acting in partnership with

socio-economic and moral arguments. The child labor reform movement of the early Progressive Era can be seen as a turning point. Before then reformers relied mainly on moral admonition. Afterwards, they harnessed scientific evidence of the biological and psychological vulnerability of the young and the benefits of preventing harmful exposures. Of special note, as we have seen, the 19th century reformers understood and wrote about the lifecourse and transgenerational impacts of toxic chemicals and psychosocial stressors. Their understanding was based on empirical data. Scientific research in the last decades has now revealed that early epigenetic alterations occurring during fetal development as a result of environmental or psychosocial insults can permanently reprogram the functional capacity of organs--with effects seen in childhood, adulthood and in future generations (see (F. Perera & Herbstman, 2011) for review; (Bagot & Meaney, 2010; Bauer & Boyce, 2004; Curley & Mashoodh, 2010; Jirtle & Skinner, 2007; Li et al., 1997; Oberlander et al., 2008; Skinner & Guerrero-Bosagna, 2009)). In echoes from the 19th century, this scientific evidence is fueling new efforts to reform policy to protect children's health (Rothstein, Yu, & Marchant, 2009; *Toxic Chemicals and Vulnerable Populations: Moving Forward with New Opportunities*, 2008).

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Paper 2

Interaction between Prenatal Exposure to Airborne Polycyclic Aromatic Hydrocarbons and Maternal Psychological Distress in Pregnancy on Child Behavior

Running/Short Title: Exposure to Airborne PAH, Maternal Distress and Child Behavior

Acknowledgement: Thanks to the U.S. Centers for Disease Control and Prevention in Atlanta, GA, for their analysis of cotinine and urinary PAH metabolites.

Conflicts of Interest: None

Keywords: Prenatal, PAH, air pollution, child behavior, maternal psychological distress, demoralization

Abbreviations: ADD, attention deficit disorder; ADHD, Attention deficit hyperactivity disorder; B[*a*]P, benzo[a]pyrene; BDNF, brain-derived neurotrophic factor; CBCL, Child Behavior Checklist; CI, confidence intervals; CCCEH, Columbia Center for Childrenõs Environmental Health; ETS, environmental tobacco smoke, DSM, Diagnostic and Statistical Manual of Mental Disorders; FEBAD, fetal- basis- for- adult- disease , GR, glucocorticoid receptor; HDAC, histone deacetylatase; HLEE, health, lifestyle, and environmental exposure; HOME, Home Observation for Measurement of the Environment; LTP, long-term potentiation; NMDA, N-methyl- D ï aspartate; PAH, polycyclic aromatic hydrocarbons; PERI-D, Psychiatric Epidemiology Research Instrument-Demoralization; PUF, polyurethane foam; QC, quality control; SAM, sympathetic-adrenomedullary,

Abstract

Background: Airborne polycyclic aromatic hydrocarbons (PAH) are widespread neurotoxic urban pollutants generated by burning of organic material including fossil fuel such as coal, diesel and gasoline. Psychosocial stressors are also prevalent. Both prenatal PAH exposure and maternal psychological distress during pregnancy have been associated with neurodevelopmental problems in children. However, less is known about the potential interactions between these factors that may put children at greater risk of behavioral problems that affect learning and academic success.

Objective: The goal was to evaluate the potential interactions between maternal exposure to airborne PAH and maternal psychological distress during pregnancy on subsequent behavioral problems in children.

Methods: In a longitudinal birth cohort study, children of nonsmoking Caucasian women in Krakow, Poland were followed from *in utero* until 9 years of age. Prenatal PAH exposure was measured by personal air monitoring of the mothers during pregnancy. Maternal demoralization during pregnancy, a measure of psychological distress, was assessed by the Psychiatric Epidemiology Research Instrument-Demoralization (PERI-D). Child behavior was assessed by the Child Behavior Checklist (CBCL) at age 6 to 9. The interactions between maternal demoralization and prenatal PAH exposure on neurobehavioral outcomes were evaluated using Poisson and logistic regression models, adjusting for confounding variables.

Results: Significant interactions between maternal demoralization and PAH exposure (high/low) were identified for the symptoms of anxious/depressed (ƀ=0.35, p=0.023), withdrawn/depressed (ƀ=0.81, p=0.003), social problems (ƀ=0.4, p=0.051), aggressive behavior

(ƀ=0.5, p=0.0004), internalizing problems (ƀ=0.44, p=0.0002), and externalizing problems (ƀ=0.48, p<0.0001). Within the high PAH exposure group, significant maternal demoralization was significantly associated with symptoms of anxious/depressed (ƀ=0.53, p<0.0001), withdrawn/depressed (ƀ=0.83, p<0.0001), rule-breaking (ƀ=0.47, p<0.0009), aggressive behavior (ƀ=0.56, p<0.0001), social problems (ƀ=0.7, p<0.0001), internalizing (ƀ=5.01, p<0.0002), externalizing (ƀ=4.09, p<0.0005) as well as on somatic complaints (ƀ=0.88, p<0.0001), attention problems (ƀ=0.31, p=0.028) and rule-breaking behavior (ƀ=0.47, p=0.009). Fewer effects of maternal demoralization [only somatic problems (ƀ=0.38, p=0.038), social problems (ƀ=0.32, p=0.016), and attention problems (ƀ=0.25, p=0.014) were observed in the low PAH exposure group.

Conclusion: Maternal demoralization during pregnancy appears to have a greater effect on child neurobehavioral development among children who experienced high prenatal PAH exposure compared to less environmentally exposed children. The results provide the first evidence of an interaction between prenatal exposure to maternal demoralization and air pollution on child neurobehavioral development, indicating the need for a multifaceted approach to prevention of developmental problems in children.

Introduction

The specific research question addressed is whether demoralization during pregnancy has a greater adverse effect on neurobehavior among children who are more highly exposed to air pollutants during gestation than among those with low exposure.

Exposures to diverse pollutants and psychosocial stressors during pregnancy have been shown independently to adversely affect child development. Less is known about the potential interactions between these factors that may put children at greater risk of cognitive or behavioral problems that affect learning and academic success. This is an important gap in research since these factors commonly co-occur (Morello-Frosch, Zuk, Jerrett, Shamasunder, & Kyle, 2011). A better understanding of their joint effects could lead to multifaceted prenatal interventions to prevent developmental disorders in children. Such interventions would combine measures to reduce toxic exposures with the provision of psychological and material support to pregnant women experiencing high levels of stress and demoralization. The original research described in this paper addresses this research gap by providing new empirical data on the interaction between common combustion-related air pollutants (polycyclic aromatic hydrocarbons or PAH) and maternal demoralization experienced during pregnancy.

By way of context, neurodevelopmental disorders such as ADHD, learning disorders, or intellectual disability affect 12% of children in the U.S. ages 3 to 17 years (Pastor & Reuben, 2008). Neurodevelopmental behavioral and intellectual disorders are also increasingly prevalent in Europe (Wittchen et al., 2011). Many studies have shown heightened biological and psychological susceptibility of the developing fetus both to environmental pollutants and to psychosocial stressors. Differential susceptibility during fetal development is attributed to the immaturity of fetal enzymatic detoxification and DNA repair systems, the rapid differentiation of major brain structures, extensive reprogramming of epigenetic patterns, and the limited

protection provided by the blood brain barrier (Anderson, Diwan, Fear, & Roman, 2000; Grandjean & Landrigan, 2006; National Research Council, 1993; F. P. Perera et al., 2004; World Health Organization, 1986).

PAH including benzo[a]pyrene (BaP), a representative PAH, are ubiquitous air pollutants generated by combustion sources that include diesel- and gasoline-powered motor vehicles, coal-fired power plants, residential coal and oil heating, and tobacco smoking (Bostrom et al., 2002). An estimated > 80% of airborne PAH results from the combustion of fossil fuels and biomass (Bostrom et al., 2002). Although Krakow is a relatively high pollution area, it is within the range seen in other urban areas worldwide. Comparison of monitored BaP levels across urban areas worldwide shows that the annual mean ambient BaP level in various locations within Krakow, Poland, ranged from 4 to10 ng/m^3 during 2002. This level was comparable to the winter means reported in Teplice (7.42 ng/m^3) and Prachatice (5.37 ng/m^3), Czech Republic, between 1993 and 1994 (Binková, Veselý, Veselá, Jelínek, & Srám, 1999) but higher than the summer means in these cities. Pollution levels in Krakow were lower than those measured in Tongliang, China, between 2002 and 2003 (mean 15 ng/m^3) (Chow et al., 2006). In U.S. cities, as well as in many urban areas of Europe, ambient BaP concentrations range between 1 and 5 ng/m^3 during winter and in areas with heavy traffic (Naumova et al., 2002; Tonne, Whyatt, Camann, Perera, & Kinney, 2004).

As PAH are lipid soluble, they accumulate in adipose tissue and are transferred across the placenta and the fetal blood brain barrier (Brown et al., 2007; Hood, Nayyar, Ramesh, Greenwood, & Inyang, 2000). Following gestational exposure, PAH such as BaP have been shown to exert genotoxicity (F. P. Perera, Tang, Whyatt, Lederman, & Jedrychowski, 2005), epigenetic toxicity (F. Perera & Herbstman, 2011), and endocrine disruption (Liu et al., 2008; Widerak et al., 2006; Wu, Ramesh, Nayyar, & Hood, 2003) as well as to affect immune, metabolic, and neurological functions, with consequences potentially manifesting throughout the life-span (Barker, 2004; Kim, 2004; Pinkerton & Joad, 2006; Schwartz, 2004). In two parallel

prospective studies by the Columbia Center for Childrenôs Environmental Health (CCCEH), one in New York City (NYC) and one in Krakow, Poland, prenatal exposure to PAH has been associated with adverse cognitive outcomes at age 5 (Edwards et al., 2010; F. P. Perera et al., 2009). An association was also found with behavioral problems, including anxiety and depression at age 6-7, in NYC (F. P. Perera et al., 2012). Laboratory studies exposing experimental animals to PAH during the prenatal and neonatal periods have reported neurodevelopmental and behavioral effects of PAH, including anxiety, depression-like symptoms, and memory impairment in the absence of other overt toxicological effects (Saunders, Das, Ramesh, Shockley, & Mukherjee, 2006; Saunders, Ramesh, & Shockley, 2002; Saunders, Shockley, & Knuckles, 2003; Takeda, Tsukue, & Yoshida, 2004; Wormley, Ramesh, & Hood, 2004; Yokota et al., 2009). Anxiety and depression are internalizing problems known to affect learning (Emslie, 2008; J. J. Wood, 2006). Prenatal treatment of rats with BaP impaired memory and ability to learn, which is consistent with alterations in the expression profile of key genes involved in long-term potentiation (LTP), one of the major cellular mechanisms that underlies learning and memory (Brown et al., 2007; Wormley et al., 2004). Fetal BaP exposure also influenced the expression of nuclear transcription factors that mediate the onset of neuronal cell differentiation, suggesting that there may be widespread effects of this agent in the developing brain, ultimately contributing to neurobehavioral impairment (Hood et al., 2000).

The specific mechanisms by which environmental toxicants such as PAH might affect the developing brain are not fully understood. Some studies have shown that fetal toxicity may be caused by endocrine disruption (Archibong et al., 2002; Bui, Tran, & West, 1986; Takeda et al., 2004), binding to receptors for placental growth factors resulting in decreased exchange of oxygen and nutrients (Dejmek, Solansky, Benes, Lenicek, & Sram, 2000), binding to the human Ah (aryl hydrocarbon) receptor to induce P450 enzymes (Manchester, Gordon, Golas, Roberts, & Okey, 1987), DNA damage resulting in activation of apoptotic pathways (Meyn, 1995; Nicol, Harrison, Laposa, Gimelshtein, & Wells, 1995; K. A. Wood & Youle, 1995), epigenetic effects

(Wilson & Jones, 1983), and/or oxidative stress due to inhibition of the brain antioxidant scavenging system (Saunders et al., 2006). Regarding the specific effects of gestational PAH exposure on neurodevelopment of laboratory animals, potential mechanisms include impairment in N-methyl- D -aspartate (NMDA) receptor NRI subunit expression and impaired LTP generation (reviewed in (Schroeder, 2011)). In addition, low nontoxic levels of BaP have been shown to impair the neurodifferentiation of cultured neuronotypic PC12 cells, suggesting that BaP may also have direct actions on developing neuronal cells with consequences for brain maturation and development (reviewed in (Schroeder, 2011)).

Epidemiological studies have found that socioeconomic and psychosocial factors also affect fetal and child development. For example, numerous studies have found race/ethnicity to be a risk factor for low birth weight (Teitler, Reichman, Nepomnyaschy, & Martinson, 2007). Maternal depression and pregnancy-related anxiety, respectively, have been linked to preterm birth and/or low birth weight (Grote et al., 2010; Orr, Reiter, Blazer, & James, 2007). Poverty, maternal mental health and education are reported to be key determinants of neurobehavioural and intellectual development (To et al., 2004). For example, maternal education level has been positively related to child IQ (Breslau et al., 2001; Rahu, Rahu, Pullmann, & Allik, 2010). Reasons for this link may include both genetic (parental IQ) and environmental factors, such as parents being actively involved with their childôs intellectual development and encouraging educational attainment (Lawlor et al., 2006). In research focusing on the prenatal window of development, negative maternal life events measured during the first period of pregnancy (15ï 17 weeks) predicted lower scores on the 6-year-old childôs attention/concentration index (Gutteling et al., 2006). Prenatal maternal stress has been negatively associated with childrenôs verbal intelligence and language-related abilities at 5.5 years of age (Laplante, Brunet, Schmitz, Ciampi, & King, 2008). In a sample of poor minority women (some of whom were cocaine users during pregnancy), severity of maternal psychological distress was predictive of child mental development but not psychomotor development (Singer et al., 1997). Intrauterine exposures to

biological and psychosocial stress contributed to developmental impairment independently of preterm birth or growth restriction (Sandman, Davis, Buss, & Glynn, 2012).

Regarding mechanisms, in laboratory studies of experimental animals, pre- and postnatal stress exposure has been associated with changes in NMDA receptor expression in the hippocampus and frontal cortex and reduced brain-derived neurotrophic factor (BDNF) mRNA in the hippocampus and prefrontal cortex (Sandman et al., 2012). Weaver, Meany, Szyf, and colleagues (Weaver et al., 2005; Weaver, Meaney, & Szyf, 2006) showed that maternal stress and subsequent nurturing behaviors altered the epigenotype in rodent offspring, affecting their glucocorticoid receptor (GR) expression and behavior. The epigenetic changes could be reversed in adulthood by administering methionine or histone deacetylatase (HDAC) inhibitor. Possible mechanisms in humans include increases in prenatal maternal cortisol (a proportion of which passes through the placenta (Sandman et al., 2012)) and reduced activity of placental 11beta -HSD2 (placental enzyme that regulates fetal exposure to maternal cortisol) (O'Donnell, O'Connor, & Glover, 2009). Glucocorticoid receptors are present throughout the CNS; and glucocorticoids (the most important of which is cortisol) easily pass through the blood-brain barrier and influence multiple brain regions, including, but not limited to, the hippocampus, amygdala and prefrontal cortex. At high concentrations, cortisol may inhibit growth and differentiation of the developing nervous system and induce neuronal cell death, which is mediated by a decrease in BDNF. Cortisol also affects myelination in the developing brain (reviewed in (Sandman et al., 2012)). Research in humans has found that fetal exposure to elevated levels of cortisol early in pregnancy resulted in significantly lower scores on measures of mental development, whereas effects were reversed later in pregnancy (reviewed in (Sandman et al., 2012)). In children, exposure to early adversity has been associated with alterations in the sympathetic-adrenomedullary (SAM) and hypothalamic-pituitary-adrenal (HPA) neuroendocrine axes, and adrenocortical activity (Adler et al., 2005). The data indicate substantial inter-individual variability and a non-linear dose-response.

Of special concern are interactions between ñtoxicò environmental and social stressors on child health and development because they tend to cluster in the most socially disadvantaged populations (Morello-Frosch et al., 2011). However, the human evidence is limited (Chen, Schreier, Strunk, & Brauer, 2008; Clougherty et al., 2007; Cohen, Janicki-Deverts, & Miller, 2007; Rauh et al., 2004; Wright, 2009a). A number of studies show interactions between income or race and various pollutants (Chuang, Callahan, Lyu, & Wilson, 1999). Studies on blood lead and cognitive outcomes have reported an interaction of lead with various socioeconomic factors. In one study, cognitive deficits in four year old children were associated with neonatal blood lead concentrationð but only among poorer families (Dietrich, Succop, Berger, Hammond, & Bornschein, 1991). Other investigators found modifying effects of parental occupational and educational achievement on the relationship between blood lead and child cognitive development (Winneke & Kraemer, 1984). Research by the CCCEH in New York City found a significant interaction between prenatal exposure to environmental tobacco smoke (ETS) and material hardship, such that children with both ETS exposure and material hardship exhibited the greatest cognitive deficit at two years of age (Rauh et al., 2004).

The mechanisms by which maternal prenatal distress might interact with PAH exposure on neurodevelopment effects in children have not been well characterized. Better understanding of these complex interdependencies may help explain and ultimately prevent health disparities (Wright, 2009b). Adding to the importance of understanding these interdependencies is the increasing recognition that biological insults incurred in early development can play out over the entire life-course and even be heritable across generations (reviewed in (F. Perera & Herbstman, 2011)). The fetal-basis-for-adult-disease (FEBAD) hypothesis has been supported by evidence that intrauterine and environmental factors can cause serious consequences in later life by permanently reprogramming the functional capacity of organs. Classical examples include the association of low or lower birth weight with increased risk of adult onset cardiovascular disease (Bateson et al., 2004), type 2 diabetes mellitus, osteoporosis (Dennison

et al., 2001), depressive disorders (Thompson, Syddall, Rodin, Osmond, & Barker, 2001), and certain cancers (Ho, Tang, Belmonte de Frausto, & Prins, 2006). Compelling evidence now exists that epigenetic dysregulation underlies certain observed associations between adult disease and adverse environmental/nutritional conditions early in development (Heijmans et al., 2008; Joss-Moore & Lane, 2009). Further, an increasing body of evidence indicates that prenatal exposure to diverse pollutants or stress alters epigenetic programming and disease risk in the F_1 and even F_2 and F_3 generations (reviewed in (Anway, Leathers, & Skinner, 2006; Anway, Memon, Uzumcu, & Skinner, 2006; Bruner-Tran & Osteen, 2010; Curley & Mashoodh, 2010; Jirtle & Skinner, 2007; Li, Langholz, Salam, & Gilliland, 2005; F. Perera & Herbstman, 2011; Salian, Doshi, & Vanage, 2009)). The evidence indicates that both biological and psychosocial sources of stress have significant influences on the fetus with long-term consequences in the infant, child and perhaps beyond (Sandman et al., 2012). As reviewed by Bauer and Boyce, the term ñbiological embeddingòhas been used to refer to the processes by which early experiences are transformed into the expression of genes, the activation of physiological systems, and the calibration of biological set points, fundamentally altering trajectories toward health or disease over the lifespan (F. P. Perera et al., 2012).

The present analysis was undertaken within a longitudinal birth cohort study in a Caucasian population in Krakow, Poland, with relatively high but variable levels of air pollution (H. Choi et al., 2006). A major source of PAH air pollution during the study period was coal-burning in small furnaces for domestic heating (Lvovsky, Hughes, Maddison, Ostro, & Pearce, 2000). Automobile traffic emissions and coal combustion for industrial activities were less important contributors (Junninen et al., 2009). Exposure to PAH is highly variable among women in the study as evidenced by personal air monitoring during pregnancy (mean, 20.7 ng/m^3; range 1.8-323.76). The monitored levels mainly reflected ambient concentrations of the pollutants (Hyunok Choi, Wang, Lin, Spengler, & Perera, 2012). However, the population was relatively homogeneous with respect to education (90% have high school education or higher),

and marital status (93% of women were married). Moreover, although there is variation in material hardship (lack of adequate food, money for rent or heating, or clothing during pregnancy) across the population, no women experienced severe hardship (observed scores ranged from 0-2 on a scale of 0-4 where 4 is the most severe). The levels of demoralization were also moderate (mean of 1.01, range 0.074-2.52). (The possible scores range from 0-4). For comparison, the mean level of demoralization in the CCCEH New York City cohort was 1.16, with a range of 0-3.30). These population characteristics gave us an opportunity to assess modification of PAH effects by maternal psychological distress, within a population not experiencing extreme disadvantage or extreme psychological distress.

Psychological distress or demoralization is a major public health problem in its own right (de Figueiredo & Frank, 1982) and has been linked with measures of socioeconomic status (Hope, Power, & Rodgers, 1999). Maternal psychological distress during pregnancy has been associated with low birth weight and prematurity, with some evidence of interaction between distress and maternal smoking on birth outcomes (Bolten et al., 2011). The Psychiatric Epidemiology Research Instrument-Demoralization (PERI-D) (B. S. Dohrenwend, Krasnoff, Askenacy, & Dohrenwend, 1978) is a standardized measure of nonspecific psychological distress (demoralization) which has been used in a large number of previous studies of stressful living conditions (B. P. Dohrenwend, Shrout, Egri, & Mendelsohn, 1980). Psychological distress, or demoralization, represents the individualôs response to ñstressò, where ñstressòdescribes objective measures such as adverse socioeconomic conditions and negative maternal life events. We can consider the objective measures of stress to be the causes of demoralization which then communicates itself to the developing fetus (i.e., demoralization is the hypothesized proximate cause of behavioral effects in the child) (B. Dohrenwend, personal communication). Studies have shown that the PERI-D scores are elevated for depression, anxiety, post-traumatic stress disorder, and a host of psychiatric outcomes; however, all the subscales are highly correlated. Therefore, the PERI-D provides a general screen for many kinds of psychiatric

outcomes (B. Dohrenwend, personal communication). The PERI scales were not developed to yield specific clinical diagnoses (B. P. Dohrenwend et al., 1980). The choice of this instrument was based on our interest in assessing the effects of general psychological distress as a modifying factor, rather than in obtaining clinically diagnosable outcomes such as depression. In the CCCEH New York City cohort study prenatal and postnatal demoralization levels were highly correlated (Reyes et al., 2011) (Spearman v: $p<0.01$, 1, 2, 3 and 5 years after delivery), indicating that the PERI-D provides a measure of general (non-pregnancy related) psychological distress.

In order to determine whether there were identifiable specific social and economic factors that led to demoralization in this cohort and would potentially offer opportunities for intervention, correlations were examined between demoralization and the specific objective measures of stress reported during pregnancy: maternal education and material hardship.

The limitations of this study to investigate all possible alternative explanations and to fully account for postnatal exposures including maternal demoralization are described in the Discussion. Because the Krakow population is Caucasian and genetically homogeneous, competing explanations such as race/ethnicity and genetic variation were effectively ruled out. As the study included only non-smoking women, active maternal smoking was also not a factor; and ETS exposure was included as a covariate in the models. To the extent possible given limitations of the data, postnatal exposures to ETS air pollution were considered as covariates in the models.

Methods

Sample selection:

The study was approved by the ethics committee of the Jagiellonian University and the Institutional Review Board of the New York Presbyterian Medical Center. Informed consent was obtained from all subjects. Nonsmoking, pregnant women residing in the Srodmiescie (Old Podgorze) and the Krowodrza-Nowa Huta (New Podgorze) areas were recruited between November 2000 and March 2003 (W. Jedrychowski et al., 2004). Pregnant women were eligible if they were not currently smoking, registered at prenatal health care clinics in either of the two target areas, had lived at the present address for at least a year before the initial interview, were between the 8th and 24th weeks of gestation, were >18 years of age, had no current occupational exposure to PAH or other known developmental toxicants, had no history of illicit drug use, pregnancy-related diabetes, or hypertension, and had a valid estimate of gestational age.

Personal Interview, medical record, and biomarker data:

Between the 20th and 30th week of pregnancy, research workers administered an in-depth health, lifestyle, and environmental exposure (HLEE) questionnaires to all women in their homes. On completion of the interview, 48-hr personal air monitoring was carried out. To examine consistency in self reporting, the interview was repeated during the third trimester. After delivery, data on pregnancy and delivery were obtained from the mothersôand infantsô medical records.

The HLEE questionnaire was administered by a trained interviewer to obtain demographic information, health and environmental data. The questionnaire elicited information on ETS exposure during pregnancy (presence/absence of smokers in the household during pregnancy), dietary PAH (frequency of consumption of broiled, fried, grilled, or smoked meat during pregnancy), and socioeconomic information related to income and education. Postnatal interviews were administered to mothers every 6 months after birth to determine any changes in

residence, exposure to ETS or other health or environmental conditions. As previously reported, to validate self-reported exposure to ETS during pregnancy, cotinine in cord plasma PAH was analyzed at the Centers for Disease Control and Prevention (CDC)(Edwards et al., 2010). PAH metabolites in child urine collected at age 3 were also analyzed by CDC, creatinine-adjusted, and used as a measure of postnatal PAH exposure (Edwards et al., 2010).

Psychiatric epidemiology research interview demoralization scale and maternal intelligence:

The PERI-D was administered to the mothers during the second trimester to evaluate maternal psychological demoralization over the last year. The instrument is comprised of 27 questions to assess eight domains (perceived physical health, sadness, poor self-esteem, dread, anxiety, confused thinking, hopelessness/helplessness, and psychophysiological symptoms). Each question is rated on a 5- point likert scale (scored 0 to 4), where a higher score indicates greater demoralization (B. S. Dohrenwend et al., 1978).

Maternal intelligence was assessed using the Test of Nonverbal Intelligenceï Third Edition (TONI-3), a language-free measure of general intelligence considered to be relatively free of cultural bias (DeMauro, 2001).

Prenatal personal PAH assessment:

Forty-eight hour personal air monitoring was carried out during the second or third trimester as previously described (H. Choi et al., 2006). During the daytime hours for two consecutive days, the women wore small backpacks holding personal air monitors and kept the monitors near their beds at night to determine their inhalation exposure to PAH. The sampling

inlet was close to the woman's breathing zone. Pumps operated continuously at 2 L/min, collecting semivolatile vapors and aerosols. Vapors and particles of ≤2.5 µg in diameter were collected on a pre-cleaned quartz microfiber filter and a pre-cleaned polyurethane foam cartridge backup. The samples were analyzed at Southwest Research Institute (SWRI) for benz[a]anthracene, chrysene, benzo[b]fluroanthene, benzo[k]fluoroanthene, BaP, indeno[1,2,3-cd]pyrene, disbenz[a,h]anthracene and benzo[g,h,i]perylene. For quality control (QC), each personal monitoring measurement was assessed as to accuracy in flow rate, time, and completeness of documentation of samples. Those not meeting QC criteria for adequacy were excluded from analysis (H. Choi et al., 2006). The 48-hour personal monitoring was validated as an indicator of longer-term, integrated exposure by simultaneously monitoring a subset of pregnant women (n=80) for personal, indoor, and outdoor airborne PAH concentrations. These three measurements were found to be highly correlated (pair-wise Spearmanõs coefficients Ó 0.84, p< 0.01) (H. Choi et al., 2008) supporting the use of personal monitoring to integrate indoor and outdoor exposure.

Behavioral Outcomes:

A research worker trained in neurodevelopmental testing administered the CBCL to the mothers at child ages 6 to 9. The CBCL (Achenbach & Rescorla, 2000; Achenbach & Rescorla, 2001) has been widely used and has been shown to be sensitive to diverse prenatal exposures, including stress events during pregnancy, maternal ethnicity, smoking during pregnancy, and exposure to PAH, pesticides, methylmercury, and tobacco smoke (Axtell et al., 2000; Robinson et al., 2008; Wasserman, Liu, Pine, & Graziano, 2001). The CBCL syndromes include problems and complaints in the areas of Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-breaking Behavior, Aggressive Behavior, and the summary composite scales of Internalizing and Externalizing problems. The

syndrome scores were computed for each domain of interest by summing the scores on the specific items, with higher scores indicating more symptoms. The CBCL further yields scales derived from the *Diagnostic and Statistical Manual (DSM) of Mental Disorders* (2000) that are intended to approximate clinical diagnoses. The DSM scores are dichotomized using a ñborderline or clinicalò cut-point corresponding to the 93rd percentile for each domain. The syndrome scores are converted into T- scores by assigning a score of 50 to those with percentiles of raw scores Ò50 based on a reference population (Achenbach & Rescorla, 2001; Petersen, Kolenm, & Hoover, 1993), then dichotomized using a ñborderline or clinicalò cut-point corresponding to the 93rd percentile for each domain. For both the syndrome and the DSM scores, children are classified as in the borderline or clinical range (T- scoreÓ65; DSM scoreÓ565) or in the normal range (T score <65; DSM score <65). **Table 2** shows the distribution of behavioral outcomes in the sample.

Statistical Analysis:

As in prior analyses (H. Choi et al., 2006; Edwards et al., 2010), a composite (total) PAH variable was computed from the eight inter-correlated PAH air concentration measures (r values ranging from 0.34-0.94; all p-values < 0.001 by Spearman's rank). The primary PAH exposure variable in the analysis was total PAH dichotomized at the median value in the parent population (22.11 ng/m^3) to obtain a measure of high/low exposure. Dichotomized PAH was considered preferable to the continuous variable because it is less vulnerable to measurement error at the extremes of exposure. PAH.(Ln transformed) was used in a secondary analysis of the interaction in order to compare results using the two different variables. Maternal demoralization was treated as a continuous variable.

To determine whether the two exposures of interest may have a common antecedent or be otherwise interrelated, the correlation between prenatal PAH exposure and maternal demoralization was examined. Correlations between maternal demoralization on the one hand and material hardship, maternal education, or income were also analyzed to assess whether any of these factors could be causally related to maternal demoralization. Pearson, Spearman rank order correlation, or Chi-square was used as appropriate depending on whether continuous or categorical variables were analyzed.

The Poisson regression model was applied on the raw (untransformed) CBCL syndrome scores because they are count data that sum the scores on the specific items within each scale; and the score distribution for each syndrome is right-skewed. Internalizing and externalizing problems were analyzed using linear regression models. Dichotomized T-scores and DSM scores were analyzed using logistic regression. Covariates were selected if they were of *a priori* interest based on the literature or our previous studies and also were significant contributors to at least one of the outcomes.

The covariates included childôs age at assessment (in months), season at the time of monitoring [heating (October-April) versus non-heating season (May-September)], gestational age, ETS exposure during pregnancy, sex, and motherôs education (completion of Lyceum or high school prior to birth of the child). As in prior analyses, maternal education was used as a proxy for socioeconomic status (Edwards et al., 2010). As income was indirectly measured by income tax level and 26% of women either did not know or refused to answer the question, income was not considered a reliable socioeconomic variable and was not included as a covariate. Dietary PAH exposure was not correlated with monitored PAH and was not a significant predictor of CBCL scores ($p < 0.1$) and thus was not included as a covariate. Because prenatal PAH exposure was found previously to be associated with reduced birth weight in this cohort (H. Choi, Rauh, Garfinkel, Tu, & Perera, 2008), we evaluated its potential as a confounder and possible mediator by including birth weight in separate models. Maternal

intelligence is a known correlate of child cognitive development (Kagan & Moss, 1959; Noble & McCandliss, 2005) but was available only in a subset of the children, therefore it was included with the other covariates in a secondary analysis. We also adjusted for postnatal PAH exposure using the sum of creatinine-adjusted PAH metabolites in urine collected at 3 years of age or a measure of postnatal change of residence as an indicator of likely, although unmeasured, change in exposure to airborne PAH after birth. We further adjusted for maternal report of postnatal exposure to ETS in the home. These latter models were limited by the smaller numbers of participants with data on these additional covariates.

To investigate the interaction between the two exposures of interest, an interaction term [prenatal PAH exposure (dichotomous) x maternal demoralization (continuous)] was incorporated into regression models. This treatment of our key independent variables allowed us to examine the differential effects of demoralization within the high vs. the low exposure groups. Interactions between the objective measures of stress (low level of education and material hardship) were explored in separate models in order to compare their combined effect with that between the proximate psychosocial factor (demoralization) and PAH. In addition, separate models were run including multiple interaction terms: 1) PAH x maternal demoralization and PAH x material hardship; 2) PAH x maternal demoralization and PAH x maternal education, and 3) all three interaction terms, to determine whether the results for the interaction of primary interest remained after their inclusion.

Stratified analyses were conducted to assess the effects of maternal demoralization within the high and low PAH exposure subgroups. Although interactions were of primary interest, we also report the main effects of PAH and distress on the behavioral outcomes, using the same models without the interaction terms.

All effect estimates and p-values (Ŭ set at 0.05) were generated using SAS (version 9.1.0.3; SAS Institute Inc., Cary, NC, USA).

Results

Four hundred twenty-three participants had complete PAH monitoring data, medical record and questionnaire data (including prenatal and postnatal exposure to ETS, residential history, sex, maternal high school completion and gestational age). Of these children, 248 had complete questionnaire and CBCL data at age 6-9 and were included in the present analysis.

Table 1 shows the characteristics of the subset of the 248 children included in the analysis (having adequate data on prenatal PAH exposure, CBCL and required covariates). There were no significant differences in these characteristics between the children who were included in the analysis and those not included because they had not reached the age of 9, had missed this particular developmental assessment or were lost to follow-up (n=75). As reported previously, all mothers in the study had detectable levels of PAH in prenatal personal air samples, while 35.5% reported ETS exposure during pregnancy (Edwards et al., 2010). The mean PAH concentration was higher in the winter/heating season than the summer/non-heating season. For example the winter mean concentration of BaP was 4.9 ng/m^3 compared to 0.9 ng/m^3 in the summer) (W. Jedrychowski et al., 2007)

Table 2 shows the distribution of behavioral outcomes in the cohort. A relatively small percentage of children had syndrome scores in the borderline or clinical range (8.4-12%). PAH exposure and maternal demoralization treated as continuous variables were not significantly correlated, either in the overall cohort ($r=0.054$, $p=0.267$) or in the subset analyzed ($r=0.016$, $p=0.80$). Neither material hardship nor maternal education was correlated with PAH, either in the overall cohort or in the subset analyzed (all $p>0.2$). Maternal education years of education) was inversely correlated with demoralization in the subset analyzed (-0.12, $p=0.057$) but not in the entire cohort. In the overall cohort, but not the subset analyzed, material hardship was positively correlated with maternal demoralization ($r=.18$, $p<0.001$). These results suggest that maternal education and material hardship may be predictors or antecedents of demoralization.

Correlations between airborne PAH and ETS exposure and between airborne PAH and dietary PAH were not significant, either in the cohort as a whole or the subset studied here (all $p<0.12$). As reported previously, ETS exposure during pregnancy was significantly correlated with maternal and cord cotinine levels both in the entire cohort. Among the entire cohort, self-reported ETS exposure during pregnancy was correlated with cotinine in both cord blood and maternal blood at delivery (0.33 and 0.35, respectively; both $p< 0.0001$). Correlations were also significant within the present subset (0.30 and 0.34), supporting self-reported ETS as a reliable measure of ETS exposure (Edwards et al., 2010).

In the regression model, a significant interaction was observed between prenatal PAH exposure (high/low dichotomized at the median) and maternal demoralization (continuous measure) on the symptoms of anxious/depressed ($\beta=0.35$, $p=0.023$), withdrawn/depressed ($\beta=0.81$, $p=0.003$), social problems ($\beta= 0.4$, $p= 0.051$), aggressive behavior ($\beta=0.50$, $p=0.0004$), internalizing problems ($\beta=0.44$, $p=0.0002$), and externalizing problems ($\beta=0.48$, $p<0.0001$) (**Table 3**). (Here the betas are the interaction terms, which refer to the difference between the effect of demoralization in the high vs. the low PAH exposure groups. **Figure 1** displays the interactions more clearly by showing the effects of maternal demoralization within the high and low PAH exposures groups, separately.

Within the high PAH exposure subgroup, we found significant effects of maternal demoralization for all the problems mentioned above ($p<0.001$), and in addition, for somatic complaints ($\beta=0.88$, $p<0.0001$), attention problems ($\beta=0.31$, $p=0.028$), and rule-breaking behavior ($\beta=0.47$, $p=0.009$) (**Table 3**). In contrast, among the low PAH exposure subgroup only somatic complaints ($\beta=0.38$, $p=0.038$), social problems ($\beta=0.32$, $p=0.016$), and attention problems ($\beta=0.25$, $p=0.014$) were significantly associated with maternal demoralization (**Table 3**). **Table 4** shows the results for the T-scores for symptoms. As expected since numbers of children in the borderline or clinical range are limited, there are fewer significant results compared to the results for continuous scores in **Table 3.**

After adjusting for change of residence after the babyôs birth (as an indicator of potential change in air pollution exposure) (n=241) or for maternal intelligence) (n=199), the previously observed interactions remained significant. Further, adjusting for postnatal ETS and postnatal urinary PAH metabolites at age 3, the associations remained the same except for symptoms of anxious/depressed which were no longer significant (p=0.15) probably due to small sample size (n=112) (**Table 5**).

In logistic regression with dichotomized T-scores, significant interactions were found between prenatal PAH exposure and maternal demoralization on symptoms in the borderline or clinical range for somatic complaints (ƀ=4.37, p=0.021), aggressive behavior (ƀ=3.31, p=0.04), and externalizing problems (ƀ=6.14, p=0.019) (**Table 4**). Also using dichotomized T-scores, within the high PAH exposure group, maternal demoralization was significantly associated with anxious/depressed (ƀ=1.84, p=0.011), somatic complaints (ƀ=6.28, p=0.004), aggressive behavior (ƀ=3.56, p=0.019), and internalizing problems (ƀ=1.68, p=0.019). In the logistic model for DSM scores, no significant interactions were found because of the small number of subjects with scores above the ñborderline or clinicalò cut-point. However, within the high PAH exposure subgroup, maternal demoralization was associated with somatic complaints (ƀ=3.1, p=0.008).

The same analysis of the interaction of PAH x demoralization using the continuous measure of PAH (LnPAH) gave results consistent with those based on the dichotomous PAH measure (**Table 6**).

With respect to main effects of the two exposures, in the models without the interaction term (PAH x demoralization), PAH exposure was a significant predictor of symptoms of withdrawn/depressed (p=0.0015), social problems (p=0.015), aggressive (p=0.001), and externalization (p=0.044). Prenatal maternal distress was a significant predictor of symptoms of all problems with the exception of thought problems (all p<0.02) and of the T-scores for anxious/depressed, somatic, social problems, and internalization (all p<0.02).

In the models testing the interactions between PAH and material hardship the effects were not significant except for two syndrome scores (anxious/depressed and internalizing) for which the betas were negative. The interactions between maternal education and PAH were not significant. These results are shown in **Table 7. Table 8** provides the results from the models including multiple interaction terms: (1) PAH x maternal demoralization and PAH x material hardship; 2) PAH x maternal demoralization and PAH x maternal education, and 3) all three interaction terms. The interactions between PAH and demoralization remained significant in all of these models.

Discussion

As discussed in the Introduction, previous results from this cohort have indicated that prenatal exposure to PAH air pollutants during pregnancy is a risk factor for reduced child intelligence at age 5 (Edwards et al., 2010). The present analysis suggests that maternal demoralization during pregnancy interacts significantly with prenatal PAH airborne exposure level on childrenôs neurodevelopmental outcomes, including more symptoms of anxiety and depression, and that maternal demoralization has a greater effect on multiple neurobehavioral symptoms within the high PAH exposure subgroup than within the low PAH exposure subgroup as shown in **Table 3** and **Figure 1**. The results are of concern because behavioral problems such as anxiety and depression can affect childrenôs ability to learn (Emslie, 2008; J. J. Wood, 2006). Interactions between toxic physical (environmental) and ñsocialò toxicants on child health and development are of special concern because social and environmental toxicants tend to cluster in the most socially disadvantaged populations. This study suggests that, even in more advantaged populations with modest levels of socioeconomic stress, these factors may combine to adversely affect childrenôs development.

The strengths of this analysis include the ability to account for a number of factors other than PAH exposure that are known to affect child neurobehavioral development and the ability to draw upon individual prenatal exposure data from personal monitoring, biomarker data, and extensive medical record and questionnaire data. However, there are a number of important limitations to this study. Because the Home Observation for Measurement of the Environment (HOME) Inventoryð a measure of the childôs proximal caretaking environment that can confound a study on neurodevelopment (Bradley, Corwyn, & Whiteside-Mansell, 1996)ð is not widely used in central Europe, it was not administered in the Polish cohort. However, analysis adjusted for which maternal education partially accounts for the important role of the mothers in stimulating the child (W; Jedrychowski et al., 2009; Kagan & Moss, 1959; McAskie & Clarke, 1976; Noble & McCandliss, 2005). In the present study personal airborne PAH levels were not correlated with total years of education completed by the mother, either in the overall cohort or in the subset analyzed, mitigating concern that unmeasured differences in socioeconomic status may have confounded our findings on PAH exposure.

There are a number of limitations. We were not able to identify the specific sources of airborne PAH. However, all eight speciated PAH monitored have outdoor sources identified with coal combustion. Although some are also related to ETS, prenatal ETS was not correlated with monitored air concentrations of PAH, consistent with the analysis of Choi and colleagues (H. Choi et al., 2006). Relying on a single measurement of prenatal air for our exposure matrix is limiting; but simultaneous personal, indoor and outdoor monitoring of a subset of the cohort showed that the three measurements were highly correlated (H. Choi et al., 2008). Moreover, because measurements during the second and third trimesters were correlated (H. Choi et al., 2008), we considered the single monitoring time point to be a reasonable indicator of prenatal exposure via inhalation over the last two trimesters of pregnancy. Regarding the potential effect of season on our results, monitoring was evenly distributed across seasons (n = 86, 81, 85, and 92 mothers monitored in spring, summer, fall, and winter, respectively) and we adjusted for

season in the analysis. Moreover, we did not make the assumption that the second and/or third trimesters of pregnancy are the most vulnerable periods with respect to brain development. The first trimester may be equally or more important.

Further limitations of the analysis are the possibility that unmeasured co-pollutants from fossil fuel may be responsible for the observed effects of PAH in combination with demoralization. This concern is mitigated somewhat by the finding from a parallel study in New York City that both prenatal personally monitored PAH levels and PAH-DNA adducts in cord blood were associated with behavioral problems in the children (F. P. Perera et al., 2012). There is also the possibility of residual confounding by unmeasured variables and our inability to rule out all competing explanations. However, as noted in the Introduction, certain competing explanations such as race/ethnicity and genetic variation and active maternal smoking in pregnancy were effectively ruled out by design. We also addressed the competing explanation that the interactive effects of PAH and demoralization effects might be due to effects of both exposures on birth weight. Transplacental exposures to PAH have been linked to decrements in birth weight and other adverse birth outcomes, including in this cohort (H. Choi et al., 2006; Dejmek et al., 2000; F. P. Perera et al., 2003; Whyatt et al., 1998) and these decrements have been associated with lower cognitive functioning and behavioral problems in childhood (Hack et al., 1991). Maternal stress has also been associated with adverse birth outcomes (Bolten et al., 2011). Therefore, it is possible that birth weight might have been a confounder or a potential mediator of the observed effects in this study. However, in this analysis, birth weight of the newborn was not a confounder or apparent mediator of the effects of PAH in combination with maternal demoralization.

Although the fetal window is considered to be the most vulnerable to psychological stress as well as to toxic pollutants, postnatal exposures can be important contributors. A limitation is that postnatal measures of demoralization that could affect both child behavior and mothers' perception of her child's behavior were not obtained. Finally, we were not able to

assess the effect of postnatal PAH exposure through air monitoring. However, as measures of postnatal air pollution exposure, we were able to use levels of PAH metabolites in child urine or change in location of neighborhood of residence as a proxy for likely change in air pollution exposure postnatally.

Conclusion

In conclusion, this study provides evidence that the combination of high prenatal exposure to environmental PAH and maternal demoralization during pregnancy adversely affects child behavior and that maternal prenatal demoralization has a greater effect among children with high prenatal exposure than among those with lower PAH exposure for a majority of behavioral symptoms. These results are of concern since neurobehavioral problems such as reported here may affect subsequent academic performance and well-being. Given the importance of womenôs mental health during pregnancy for fetal and child development (Federenko & Wadhwa, 2004), these results suggest the need to screen women early in pregnancy to identify those in need of psychological or material support as part of a multifaceted approach that also includes policy interventions to reduce air pollution exposure in urban areas. The results suggest that concerted policies to reduce stress and pollutant exposure to pregnant women have the potential to result in benefits that are amplified beyond those of the individual policies.

As reviewed by Bauer and Boyce, the final decades of the twentieth century witnessed remarkable progress in advancing children's rights and well-being worldwide (F. P. Perera et al., 2012). Nonetheless, adverse psychosocial, economic, and environmental conditions are commonplace worldwide, affecting the health, well-being, and prosperity of individuals and

societies. Not only do children bear a disproportionate share of the burden of such adversities, but they are uniquely sensitive to the negative consequences that accompany exposures during early development. Effects of childhood adversity may persist over a lifetime and thus have implications for society as a whole. To paraphrase these authors, the key to prevention lies in a better understanding of õthe complex but tractable interactions of biology, context and early development.ò

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Table 1: Characteristics of Children Included in the Analysis and Children Not Included

	Subjects included in the analysis (n=248)		Subjects not included[a] (n=175)			P-value for difference[b]
Variable	Mean	Std Dev	Mean	Std Dev	N	
Total PAH (ng/m^3)	40.77	53.58	48.69	58.21	175	0.150
Gestational age (in weeks)	39.41	1.60	39.35	1.43	175	0.726
Maternal psychological distress score[1]	1.00	0.40	1.06	0.48	175	0.230
Age at assessment (in months)	87.39	11.81	NA	NA	0	NA
% smoking at home[2]	22.58%		19.43%		175	0.435
% female	51.21%		47.43%		175	0.444
%$\geq$ high school education[3]	91.53%		89.71%		175	0.524
Heating season[4]	52.82%		61.49%		174	0.077

[a] Of 423 children with valid prenatal monitoring and questionnaire data, 248 had CBCL data at age 6-9 and data on other required covariates. Subjects were not included due to missing data or loss to follow-up (n=175).

[b]Statistical difference between the two groups based on a two-sample t-test or a Chi-square test
[1] Maternal psychological distress during pregnancy (PERI-D)
[2]Prenatal ETS exposure in the home from smokers other than the mothers who are nonsmokers
[3]Maternal education high school or above
[4]Monitoring during the heating season (yes/no)

Table 2: Distribution of Behavioral Outcomes (Behavioral Symptoms) in the Cohort

Syndrome	Score range		Mean of scores		Percent in borderline or clinical range[b]
	T-score[a]	Raw (untransformed) score	T- score	Raw (untransformed) score	
Anxious/Depressed	50-97	0-17	55.89	3.89	12.01
Withdrawn/Depressed	50-91	0-14	54.16	1.40	6.73
Somatic Complaints	50-88	0-16	54.33	1.41	5.87
Social Problems	50-91	0-13	54.09	2.21	4.47
Thought Problems	50-76	0-11	52.33	1.23	1.40
Attention Problems	50-77	0-13	53.96	3.32	3.63
Rule-Breaking Behavior	50-84	0-31	54.22	2.82	3.36
Aggressive Behavior	50-92	0-60	53.65	5.37	6.42
Internalizing Problems	33-83	0-40	52.09	7.34	11.73
Externalizing Problems	33-94	0-160	51,01	10.02	3.91

[a] The T-score is truncated (Petersen et al., 1993); that is, a score of 50 is assigned to those with percentiles of raw scores Ò50 based on a reference population (Achenbach & Rescorla, 2001).
[b] The syndrome T-scores were dichotomized at T=65 as the cutoff for the borderline and clinical range. Internalizing and Externalizing Problems are analyzed continuously and therefore do not have a dichotomized value.

Table 3. Interaction between PAH (High/Low) and Maternal Depression Overall and the Effect of Demoralization within the High vs. Low PAH Exposure Groups[1]

	Interaction[a] (N = 248)		Within the high PAH group (N =114) [b]		Within the low PAH group (N = 134) [b]	
Syndromes	$ƀ_{interaction}$	p-Value	ƀ	p-Value	ƀ	p-Value
Anxious/Depressed	0.35	0.023*	0.53	<0.0001**	0.16	0.13
Withdrawn /Depressed	0.81	0.003*	0.83	<0.0001**	-0.05	0.77
Somatic Complaints	0.36	0.20	0.88	<0.0001*	0.38	0.038*
Social Problems	0.40	0.051*	0.70	<0.0001*	0.32	0.016*
Thought Problems	0.17	0.59	0.20	0.40	0.003	0.99
Attention Problems	0.08	0.64	0.31	0.028*	0.25	0.014*
Rule-breaking Behavior	0.42	0.06	0.47	0.009*	0.03	0.87
Aggressive Behavior	0.50	0.0004*	0.56	<0.0001*	0.01	0.92
Internalizing Problems	3.61	0.026*	5.01	<0.0002*	1.06	0.27
Externalizing Problems	3.79	0.012*	4.09	<0.0005*	0.87	0.94

[1] Results of analysis of dichotomized T-scores are provided in the text and in Table 4.
[a] Prenatal PAH dichotomized at median (22.11 ng/m^3). Models adjusted for prenatal ETS, sex, maternal high school completion, gestational age, maternal psychological distress during pregnancy (continuous measure), age at assessment, and heating season at time of monitoring
[b] Effect of maternal psychological distress (continuous) within the specified PAH exposure group
*p-Value < 0.05

Figure 1: Significant Interactions between Maternal Psychological Distress and PAH Exposure (Thick line is high exposure; thin line is low exposure)

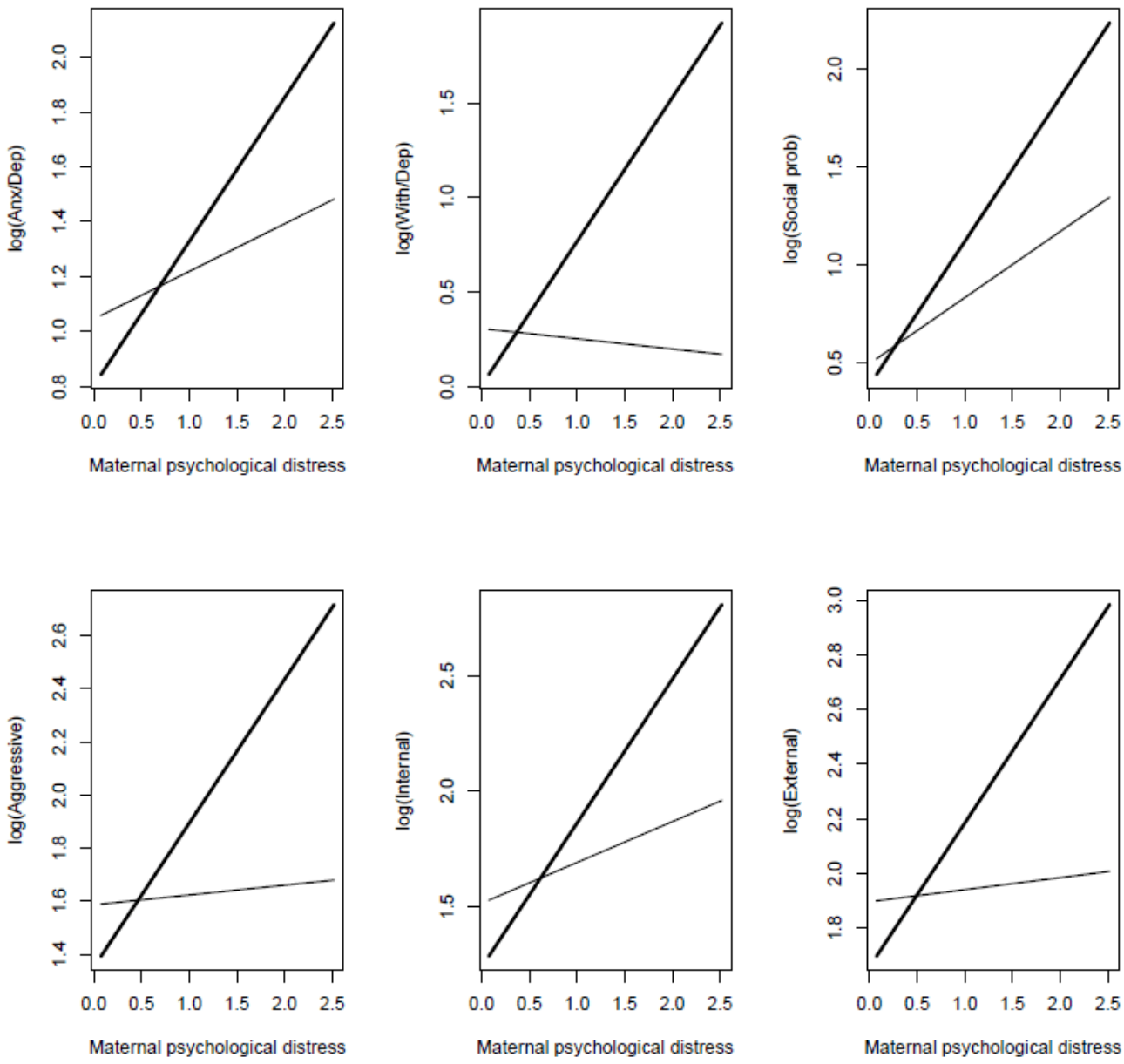

Table 4. Interaction between PAH (high/low) and Maternal Psychological Distress on CBCL Dichotomized T-Scores for Symptoms and Effects of Maternal Psychological Distress within Each PAH Exposure Group

	Interaction[a] (N = 248)		Within the high PAH group (N =114) [b]		Within the low PAH group (N = 134) [b]	
Syndromes	$ƃ_{interaction}$	p-Value	ƃ	p-Value	ƃ	p-Value
Anxious/Depressed	0.67	0.513	1.84	0.011*	0.89	0.25
Withdrawn /Depressed	1.04	0.418	0.96	0.291	-0.16	0.86
Somatic Complaints	4.37	0.021*	6.28	0.004*	0.06	0.951
Social Problems	11.02	0.149	114.0	1.0	1.8	0.076
Thought Problems	-1.83	0.6601	-4.67	0.203	-2.72	0.51
Attention Problems	0.47	0.789	1.33	0.342	1.43	0.248
Rule-breaking Behavior	-1.62	0.35	0.74	0.641	2.04	0.089
Aggressive Behavior	3.31	0.04*	3.56	0.019*	0.09	0.91
Internalizing Problems	1.07	0.262	1.68	0.019*	0.46	0.495
Externalizing Problems	6.14	0.019*	20.99	0.106	-0.38	0.726

[a] Prenatal PAH dichotomized at median (22.11 ng/m^3). Model adjusted for prenatal ETS, sex, maternal high school completion, gestational age, maternal psychological distress during pregnancy (continuous measure), age at assessment, and heating season at time of monitoring
[b] Effect of maternal psychological distress (continuous) within the specified PAH exposure group
*p-Value < 0.05

Table 5. Interaction between PAH (high/low) and Maternal Depression on CBCL with Further Adjustments

	Interaction[a] with additional adjustment for change of residence after delivery (N = 241)		Interaction[b] with additional adjustment for postnatal ETS and postnatal PAH urinary metabolites (N = 112)		Interaction[c] with additional adjustment for maternal intelligence (N = 199)	
Syndromes	$ƀ_{interaction}$	p-Value	$ƀ_{interaction}$	p-Value	$ƀ_{interaction}$	p-Value
Anxious/Depressed	0.35	0.0223*	0.30	0.15	0.52	0.002*
Withdrawn Depressed	0.83	0.0040*	0.87	0.016*	0.93	0.0016*
Somatic Complaints	0.36	0.20	0.64	0.11	0.63	0.038*
Social Problems	0.39	0.058*	0.94	0.001*	0.58	0.0083*
Thought Problems	0.16	0.62	0.33	0.41	0.50	0.16
Attention Problems	0.07	0.67	0.030	0.90	0.18	0.33
Rule-breaking Behavior	0.41	0.07	0.67	0.038*	0.52	0.036*
Aggressive Behavior	0.48	0.0007*	0.50	0.010*	0.64	<0.0001**
Internalizing Problems	3.64	0.025*	4.99	0.032*	4.89	0.0034*
Externalizing Problems	3.68	0.015*	5.33	0.011*	4.75	0.0032*

Table 6. Interaction between Ln(PAH) and Maternal Depression[1]

	Interaction[a] (N = 248)				
Syndromes	$ƀ_{interaction}$	p-Value	T-Scores	$ƀ_{interaction}$	p-Value
Anxious/Depressed	0.15	0.011*	Anxious/Depressed	0.47	0.25
Withdrawn /Depressed	0.31	0.002*	Withdrawn /Depressed	0.43	0.39
Somatic Complaints	0.06	0.60	Somatic Complaints	1.33	0.044*
Social Problems	0.15	0.062	Social Problems	1,716	0.089
Thought Problems	-0.03	0.77	Thought Problems	0.46	0.76
Attention Problems	-0.01	0.92	Attention Problems	0.29	0.68
Rule-breaking Behavior	0.02	0.79	Rule-breaking Behavior	-1.38	0.03*
Aggressive Behavior	0.15	0.007*	Aggressive Behavior	0.92	0.13
Internalizing Problems	1.25	0.043*	Internalizing Problems	.55	0.15
Externalizing Problems	0.88	0.13	Externalizing Problems	1.53	0.05*

[1] Models adjusted for prenatal ETS, sex, maternal high school completion, gestational age, maternal psychological distress during pregnancy (continuous measure), age at assessment, and heating season at time of monitoring
*p-Value < 0.05

Table 7. Interactions between PAH and Material Hardship and between PAH and Maternal Education (Separate Models)

	Interaction PAH x hardship (N = 220)		Interaction PAH x education (N =248)	
Syndromes	$ƃ_{interaction}$	p-Value	ƃ	p-Value
Anxious/Depressed	-0.64	0.037*	0.04	0.85
Withdrawn/Depressed	-1.08	0.082	0.26	0.53
Somatic Complaints	-1.29	0.082	0.38	0.44
Social Problems	-0.47	0.23	-0.27	0.38
Thought Problems	-0.43	0.53	0.06	0.90
Attention Problems	-0.26	0.50	-0.13	0.60
Rule-breaking Behavior	-0.22	0.60	-0.25	0.46
Aggressive Behavior	-0.45	0.16	0.20	0.34
Internalizing Problems	-6.22	0.038*	1.03	0.66
Externalizing Problems	-2.38	0.41	049	0.83

Table 8. Interactions between PAH and Demoralization after Including Interactions of PAH with Material Hardship and Maternal Education, Pairwise, and then All Three Interaction Terms

a. Model with PAH x Demoralization and PAH x Education

	Interaction PAH x demoralization (N = 248)		Interaction PAH x education (N = 248)	
Syndromes	Estimate	ProbChiSq	Estimate	ProbChiSq
Anxious/Depressed	0.36	0.02*	0.12	0.62
Withdrawn/Depressed	0.86	0.002*	0.45	0.28
Somatic Complaints	0.39	0.1747	0.45	0.36
Social Problems	0.38	0.06	-0.20	0.52
Thought Problems	0.18	0.57	0.10	0.84
Attention Problems	0.06	0.71	-0.11	0.66
Rule-Breaking Behavior	0.40	0.08	-0.15	0.66
Aggressive Behavior	0.54	0.0002*	0.32	0.14
Internalizing Problems	3.81	0.02*	1.87	0.42
Externalizing Problems	3.94	0.01*	1.35	0.54
T-Score				
Anxious/Depressed	0.63	0.54	-22.51	1
Withdrawn/Depressed	0.93	0.47	-21.73	1
Somatic Complaints	4.37	0.02*	4.43	1
Social Problems	10.73	0.17	-20.83	1
Thought Problems	-1.83	0.66	-2.12	1
Attention Problems	0.28	0.88	-22.64	1
Rule-Breaking Behavior	-1.63	0.35	-0.70	0.68
Aggressive Behavior	3.32	0.04*	2.73	1
Internalizing Problems	0.99	0.30	-22.20	1
Externalizing Problems	6.14	0.019*	4.26	1

b. Model with PAH x Demoralization and PAH x Material Hardship

	Interaction PAH x demoralization (N = 220)		Interaction PAH x material hardship (N = 220)	
Syndromes	Estimate	ProbChiSq	Estimate	ProbChiSq
Anxious/Depressed	0.318	0.0551*	-0.6288	0.0405*
Withdrawn/Depressed	0.7443	0.0104*	-1.0595	0.0883
Somatic Complaints	0.5941	0.0474*	-1.273	0.0861
Social Problems	0.5036	0.0218	-0.4508	0.2574
Thought Problems	0.2962	0.37	-0.4218	0.5354
Attention Problems	0.1279	0.481	-0.2478	0.5126
Rule-Breaking Behavior	0.7059	0.0043*	-0.1888	0.6494
Aggressive Behavior	0.4554	0.0029*	-0.4278	0.1839
Internalizing Problems	3.6558	0.0373*	-6.1911	0.0367*
Externalizing Problems	4.1438	0.013*	-2.3479	0.4046
T-Score				
Anxious/Depressed	0.348	0.7509	-23.8073	0.9998
Withdrawn/Depressed	1.2503	0.3594	-23.3082	0.9998
Somatic Complaints	5.099	0.016*	-23.9673	1
Social Problems	971.4242	0.9981	483.6996	0.9993
Thought Problems	-2.0327	0.6311	-2.3382	1
Attention Problems	0.3161	0.8584	0.3931	1
Rule-Breaking Behavior	0.1937	0.9262	-3.5146	1
Aggressive Behavior	3.4799	0.0483*	1.0132	1
Internalizing Problems	0.7372	0.4593	-23.3528	0.9998
Externalizing Problems	7.764	0.0249*	3.6149	1

c. Model that Includes All 3 Interaction Terms

	Interaction PAH x depression (N = 220)		Interaction PAH x education (N = 220)		Interaction PAH x hardship (N = 220)	
Syndromes	Estimate	ProbChi Sq	Estimate	ProbChi Sq	Estimate	ProbChi Sq
Anxious/Depressed	0.3345	0.0472*	0.1389	0.5735	-0.6208	0.0433*
Withdrawn/Depressed	0.8163	0.0061*	0.5408	0.2081	-1.0207	0.101
Somatic Complaints	0.6352	0.0364*	0.5226	0.3034	-1.2605	0.0893
Social Problems	0.4902	0.0276*	-0.1173	0.7247	-0.4593	0.2495
Thought Problems	0.3318	0.3233	0.3158	0.5294	-0.405	0.5521
Attention Problems	0.103	0.58	-0.1611	0.5521	-0.2653	0.4847
Rule-Breaking Behavior	0.7191	0.0046*	0.0832	0.8168	-0.1807	0.6646
Aggressive Behavior	0.4849	0.0018*	0.24	0.3029	-0.4083	0.2055
Internalizing Problems	3.9374	0.0272*	2.1162	0.3944	-6.0582	0.0409
Externalizing Problems	4.3293	0.0107*	1.3938	0.5554	-2.2603	0.4226
<u>T-Score</u>						
Anxious/Depressed	0.2736	0.8025	-22.8082	1	-24.8379	0.9999
Withdrawn/Depressed	1.129	0.4122	-22.8432	1	-25.3556	0.9999
Somatic Complaints	5.099	0.016*	4.7874	1	-23.961	1
Social Problems	971.6804	0.9981	-160.886	0.9998	322.8853	0.9997
Thought Problems	-2.0327	0.6311	-1.4324	1	-2.3376	1
Attention Problems	0.0762	0.9661	-24.1494	1	0.1332	1
Rule-Breaking Behavior	-0.1364	0.9494	-1.1257	0.5606	-3.7193	1
Aggressive Behavior	3.4799	0.0483*	2.8145	1	1.011	1
Internalizing Problems	0.617	0.5387	-22.8024	1	-24.4262	0.9999
Externalizing Problems	7.764	0.0249*	6.07	1	3.6034	1

PAPER 3

Prenatal Exposure to Airborne Polycyclic Aromatic Hydrocarbons and IQ: Estimated Cost of IQ reduction

Abstract

Introduction: To address a gap in understanding of the potential economic benefits of reducing environmental pollution, this paper estimates the increase in IQ and related lifetime earnings that would be expected in a low income urban population as a result of a modest reduction of ambient concentrations of the combustion-related pollutants, polycyclic aromatic hydrocarbon (PAH). Low income, urban populations such as analyzed here have been shown to have disproportionate exposure to air pollution. The analysis is relevant to policy, because whereas data on the costs of implementing environmental regulations to reduce air pollution are readily available, data on monetized benefits are often sparse or lacking.

PAH are common pollutants released to ambient air by combustion of fossil fuel (oil, coal, diesel, gasoline) and other organic material. We previously reported a significant association between personal air concentrations of PAH during pregnancy and reduced IQ in an inner-city birth cohort study in New York City (NYC) conducted by the Columbia Center for Childrenôs Environmental Health (CCCEH) (F. P. Perera et al., 2009).

Methods: Based on the results of the CCCEH study, here we have calculated the estimated increase in IQ corresponding to a hypothesized reduction of PAH in NYC air from the current concentration (~ 1 ng/m^3) to .75 ng/m^3.

Results: Restricting to NYC Medicaid births and using a 5% discount rate, we estimated the gain in lifetime earnings due to IQ increase for a single year cohort of $215 million. Using more conservative assumptions, the estimate was $43 million.

Discussion: This analysis supports policies aimed at reducing the level of PAH in the air in order to reduce the developmental impacts associated with PAH exposure.

Introduction

PAH are widespread urban pollutants released to the air during incomplete combustion of fossil fuel, tobacco, and other organic material (F. P. Perera et al., 2009). Although exposure is ubiquitous, urban minority populations represent high-risk groups both for disproportionate exposure to air pollution and for adverse health and developmental outcomes (Claudio, Tulton, Doucette, & Landrigan, 1999; Federico & Liu, 2003; New York City Department of Health, 1998; Olden & Poje, 1995; F. P. Perera et al., 2002; F. P. Perera et al., 2009). As reported previously, 100% of the mothers in the CCCEH NYC cohort had detectable levels of PAH in prenatal personal air samples, and 40% reported environmental tobacco smoke (ETS) exposure during pregnancy (F.P. Perera et al., 2003). Exposures during the prenatal and early postnatal stages are of particular concern because of the heightened susceptibility of fetuses and infants to diverse environmental pollutants, including PAH (Anderson, Diwan, Fear, & Roman, 2000; Grandjean & Landrigan, 2006; NRC, 1993; F. P. Perera et al., 2004; World Health Organization, 1986). In addition to their more immediate health effects, certain prenatal exposures may critically affect epigenetic programming and immune, metabolic, and neurologic functions, with consequences manifesting throughout the lifespan (Barker, 2004; Kim, 2004; F. Perera & Herbstman, 2011; Pinkerton & Joad, 2006; Schwartz, 2004). Increased susceptibility during early stages of development is attributed to higher cell proliferation rates, lower immunologic

competence, and decreased ability to detoxify chemicals and to repair DNA damage (Anderson et al., 2000; NRC, 1993; F. P. Perera et al., 2004). Laboratory experiments have indicated that the fetal brain and nervous system may be particularly sensitive to PAH (Dong, Wang, Thornton, Scheffler, & Willett, 2008; Kim, 2004; Sanyal & Li, 2007; Takeda, Tsukue, & Yoshida, 2004).

A number of PAH, such as benzo[a]pyrene (BaP), have been shown to be reproductive and developmental toxicants in experimental studies involving prenatal exposure (Archibong et al., 2002; Sanyal & Li, 2007; Wormley, Chirwa, et al., 2004). In epidemiological studies, transplacental PAH exposure or PAH-DNA adducts in cord blood have been associated with adverse birth and neurodevelopmental outcomes in NYC, European, and Chinese newborns (Choi et al., 2006; Dejmek, Solansky, Benes, Lenicek, & Sram, 2000; F.P. Perera et al., 2003; Frederica P. Perera et al., 2012; F. P. Perera et al., 1998; Tang et al., 2006). In the prospective CCCEH cohort study, prenatal exposure to airborne PAH was associated with reduced Mental Developmental Index scores and increased odds of developmental delay at 3 years of age, measured by the Bayley Scales of Infant Development (F. P. Perera et al., 2006). Increased risk of delayed motor development was seen at 2 years of age in a cohort of Chinese children exposed prenatally to PAH, principally from coal-fired plant emissions, with exposure measured by PAH-DNA adduct levels in cord blood (F. Perera et al., 2008; Tang et al., 2008). A study in the Czech Republic indicated that schoolchildren in the district of Teplice, which had higher levels of PAH and other air pollutants from coal-burning than did the comparison district, had a significantly higher rate of teacher referrals for clinical assessment (Sram et al., 1996). We previously reported significant associations between prenatal PAH exposure and child IQ/intelligence both within the CCCEH cohort and a parallel Polish cohort (Edwards et al., 2010; F. P. Perera et al., 2009).

To our knowledge this is the first study to estimate the economic benefit in terms of higher lifetime earnings from an increase in IQ due to the reduction of prenatal exposure to

PAH. A prior analysis by Weiland et al. used data from the CCCEH cohort and the Environmentally Attributable Fraction (EAF) method to estimate the cost of early intervention services to low income children with developmental delay due to prenatal PAH exposure (Weiland, Neidell, Rauh, & Perera, 2011). That analysis was based on the observed significant association between high prenatal PAH exposure and developmental delay at age 3 in the CCCEH cohort (F. P. Perera et al., 2006), Weiland et al. estimated the cost of early intervention services ï just one measure of health costs to be $13.7 million per year for Medicaid births in NYC. At the time of that analysis data on 5 year IQ were not available. The present study has the advantage of using data on an outcome that has been used in other populations and with other exposures (lead and mercury)(Grosse, Matte, Schwartz, & Jackson, 2002; Trasande, Landrigan, & Schechter, 2005) to estimate changes in lifetime earnings.

Although controversial, cost-benefit analyses (CBA) are increasingly used to make decisions about whether or not to regulate environmental contaminants (Ashford, 2004; Boardman, Greenberg, Vining, & Weimer, 2006; Revesz & Livermore, 2008). An example of a recent cost-benefit analysis is the U.S. Environmental Protection Agency (EPA) regulatory impact analysis (RIA) for the final mercury and air toxics standards for coal and oil-fired power plants (EPA, 2011). EPA calculated social costs of the regulation to be $9.6 billion and the monetized net benefits to be $27 to $80 billion, with the benefits outweighing costs by between 3 to 1 or 9 to 1 depending on the benefit estimate and discount rate used. Although the mercury-related benefit of lifetime earnings from increased child IQ was considered, most of the benefit was from the reduction of fine particulate matter ($PM_{2.5}$)- related premature mortalities. EPA did not evaluate the distribution of costs and benefits across different socioeconomic groups although they are likely to differ among the low income and non-low income populations. For example, on the benefits side, cognitive effects of air pollutants such as IQ reduction are likely to disproportionately affect low income populations, so that reduction in exposure may benefit them the most.

By focusing on a low income population of pregnant women and utilizing data from an inner-city population previously shown to be affected by prenatal PAH exposure, this paper provides new policy-relevant data.

Methods

The CCCEH Cohort Study

Children of nonsmoking black or Dominican-American women residing in Washington Heights, Harlem, or the South Bronx in NYC were followed from *in utero* to 5 years of age (F. P. Perera et al., 2009). During the third trimester of pregnancy, personal monitoring of women enrolled in the study was conducted over a 48-hour period in order to estimate prenatal PAH exposure. Vapors and particles of Ò2.5 µg in diameter were collected with precleaned quartz microfiber filters and precleaned polyurethane foam cartridges. The samples were analyzed for eight carcinogenic and potentially neurotoxic PAH including benz[*a*]anthracene, chrysene, benzo[*b*]fluoranthene, benzo- [*k*]fluoranthene, BaP, indeno [1,2,3-*cd*]pyrene, disbenz[*a*,*h*]anthracene, and benzo[*g*,*h*,*i*]perylene. Total PAH exposure was defined as the summation of these 8 PAH. Supporting the validity of the 48-hour personal monitoring of PAH, sequential two-week indoor residential monitoring (four two-week periods from the 32nd to the 42nd weeks of pregnancy) in the CCCEH cohort showed the overall mean indoor level was significantly correlated with the individual 48-hour personally monitored estimated of PAH exposure (Rundle et al., 2012). Indoor PAH concentrations reflect, to a considerable degree, the contribution of ambient PAH pollution (Choi et al., 2008).

Prenatal and postnatal questionnaires were administered to the mothers to obtain demographic, residential, history, health, and environmental data, such as information on active and passive smoking, and socioeconomic information related to income and education. A measure of the quality of the home caretaking environment (quality and quantity of stimulation

and support available to the child in the home environment) (Bradley et al., 1989) was obtained at age 3.

As previously reported (F. P. Perera et al., 2009), at 5 years of age, an experienced research worker blinded to each childôs level of exposure administered the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R), an intelligence test designed for children 2.5 years to 7.25 years of age. The WPPSI-R provides verbal, performance, and full-scale IQ scores. Scores have a mean of 100 and a SD of 15. Scores below 70 are classified as extremely low, 70 to 79 as borderline, 80 to 89 as low average, 90 to 109 as average, 110 to 119 as high average, 120 to 129 as superior, and above 130 as very superior. Not all children had reached age 5 by the time of analysis. Of the 392 children who had reached age 5 by the time of analysis, 249 English- speaking children were tested with the WPPSI-R (no comparable Spanish version was available) and had complete information on all explanatory variables.

Multiple linear regression models were used to estimate and to test the associations between prenatal PAH exposure and IQ. After adjustment for maternal intelligence and education, quality of the home caretaking environment, environmental tobacco smoke exposure (ETS) during pregnancy, child gender, ethnicity, gestational age, motherôs intelligence (measured with the TONI-3), motherôs completed years of education, and quality of the early home caretaking environment (measured with the HOME inventory) at 3 years of age, high PAH levels (above the median of 2.26 ng/m^3) were inversely associated with full-scale IQ (beta = -4.07, *P* = .007) and verbal IQ (beta= -.67, *P*= .003) scores interpret coefficients. Air monitoring data were not available to control directly for postnatal PAH exposure; however, the associations remained after controlling for changes in residence by age 3, as a proxy for variation in PAH exposure between the prenatal and postnatal periods.

Children in the high exposure group had full-scale and verbal IQ scores that were 4.31 and 4.67 points lower, respectively, than those of less-exposed children (below the median of 2.26 ng/m^3). The associations between logarithmically (Ln) transformed, continuous PAH levels

and these IQ measures also were significant (full-scale IQ: beta -3.00; *P* = .009; verbal IQ: beta -3.53; P = .002). Air monitoring data were not available to control directly for postnatal PAH exposure; however, after controlling for changes in residence by age 3 as a proxy for variations in PAH exposure between the prenatal and postnatal periods, the inverse associations between prenatal PAH levels and IQ remained significant. These results provided evidence that environmental PAH at levels encountered in NYC air adversely affect childrenôs IQ. The observed decrease in full-scale IQ was similar to that reported for children with lifetime average blood lead concentrations between 5 and 9.9 εg/dL, compared with children with lifetime average blood lead concentrations of <5 εg/dL (difference of ï 4.9 IQ points) (Jusko et al., 2008).The findings were of concern because verbal and full scale IQ scores measured with the WPPSI-R during the preschool period have been shown to be predictive of subsequent elementary school performance in a range of populations (Kaplan, 1993, 1996; Lemelin et al., 2007; Saccuzzo, Johnson, & Guertin, 1994).

We accounted for factors other than PAH exposures that are known to affect intellectual development, including the quality of the proximal caretaking environment and maternal IQ, and we assessed intelligence at an age when IQ can be measured reliably. The study had the additional advantage of being based on individual prenatal exposure data from personal monitoring, biomarker data on lead and cotinine levels, and extensive medical record and questionnaire data. However, relationships observed for low income, minority women might be different from those for women of other races or ethnic, cultural, or socioeconomic backgrounds. We also lacked postnatal monitoring data and controlled indirectly for postnatal PAH exposure. However, humans pass more biological milestones before birth than at any other time in their lives (Nijland, Ford, & Nathanielsz, 2008) and the prenatal period is highly sensitive to neurotoxic effects of environmental contaminants (Rodier, 2004). Although we were not able to account for all of the factors determining selection into neighborhoods, our ability to control for maternal IQ and education was important since selection into neighborhoods is done by adults,

and the factors operating in that selection process that would affect child IQ are likely to be related to parental education and IQ, both of which we controlled for (at least on the maternal side). Maternal IQ and education have both direct and indirect effects on child IQ (Bacharach & Baumeister, 1998).

To derive estimates of the cost of the IQ reduction attributable to prenatal PAH exposure, we followed the method used by Grosse et al. and Trasande et al. in their assessments of lead and mercury, respectively (Grosse et al., 2002; Trasande et al., 2005). We first calculated the estimated decrement in IQ corresponding to the hypothesized reduction in PAH exposure from 1 ng/m^3 to .75 ng/m^3. One ng/m^3 was selected as the benchmark because it is the mean ambient PAH level measured in several studies of outdoor/ambient air of NYC. For example, data on ambient levels of PAH in NYC and Los angeles (LA) (Pleil, Vette, Johnson, & Rappaport, 2004) and data from a single stationary air monitor at West 168th and Broadway, NYC (unpublished data, courtesy of R. Miller) showed ambient levels to be about 1 ng/m^3 in outdoor air in NYC, as well as LA. A base level of 1 ng/m^3 is also reasonable because subtracting the mean indoor level of PAH monitored during pregnancy in the women's homes (2.08 ng/ m^3) (Rundle et al., 2012) from the personal monitored mean level (3.13 ng/m^3), which reflects both indoor and outdoor PAH exposure, gives an estimated outdoor exposure concentration of .95 or ~1.00 ng/m^3.

We followed the methodology of Weiland et al. (Weiland et al., 2011) to estimate the size of the population at risk in NYC. Because of concerns about extrapolating results from a small, specialized cohort, we restricted to the Medicaid births in NYC which shared basic socioeconomic characteristics of the CCCEH cohort. The rationale is that ninety percent of the CCCEH population were on Medicaid and, although mothers from the CCCEH cohort are nonsmokers and free of risk factors for adverse birth outcomes, they are generally comparable to other Medicaid mothers in the City. We recognize that the restriction to Medicaid births is likely to underestimate the population at risk because PAH exposure may have similar biologic

impacts on other segments of the population. However, psychosocial factors related to poverty may compound the effect of PAH.

In the absence of personal monitoring data for PAH for other segments of the population in the city, we were unable to select a population known to have the same personal exposure to PAH. However, PAH exposure is ubiquitous in the urban environment from fossil fuel burning, especially traffic. This is illustrated by the data from air monitoring of $PM_{2.5}$ (of which PAH are constituents) and other pollutants by the NYC Community Air Survey (NYCCAS) in 2008-9 that showed wide distribution of pollution throughout the NYC metropolitan area (2009). While the NYCCAS monitoring data showed variability in concentrations across the metropolitan area, the levels tended to be higher in lower income areas, reinforcing our selection of the Medicaid population as our population at risk.

The total number of births in NYC in 2002 was 122,937 of which 63,640 were births to women on Medicaid (http://www.nyc.gov/html/doh/downloads/pdf/vs/2002sum.pdf and data from the NYC Department of Health and Mental Hygiene). We assumed comparable exposure to PAH during pregnancy as in the CCCEH cohort. For a single NYC birth cohort on Medicaid, we multiplied the estimated gain in IQ per hypothesized reduction in PAH exposure (above) by the estimated gain in earnings per IQ point (see **Table 1**).

For our ñbest caseò(Case 1) estimate of the benefit of reducing PAH levels, we assumed that one IQ point results in a 1.1% increase in earnings based on Grosse (Grosse, 2007) who reviewed all available studies up to 2007. He rejected the higher estimates of Schwartz (1994), who calculated that a 1-point increase in cognitive ability could raise a personôs annual earnings by about 1.8%, and Salkever (1995),who calculated that a 1-point IQ difference is associated with a roughly 2.4% difference in earnings, averaged across men and women. Grosse based his estimate on two more recent analyses that estimated the association of cognitive ability with earnings both controlling for years of schooling and not controlling for schooling. The estimates controlling for schooling represent the direct effect of ability on

earnings. The estimates from models that do not control for schooling represent the total effect of ability on earnings and implicitly include the pathways from ability to schooling and from schooling to earnings.

Heckman, Stixrud, and Urzua (2006) estimated latent variable models of earnings using data from the National Longitudinal Study of Youth 79 and measures of both cognitive and noncognitive ability. They estimated the total effect of ability on wages of 30 year old males, including the effects of cognitive ability on schooling and of schooling on wages, to be 0.9%. Grosse noted that these estimates do not incorporate the effects on hours of work and are thus likely to be an underestimate of the association of IQ with annual earnings. They also do not include women, for whom the estimated associations between earnings and observed test scores are 30-40% larger than for men. Finally, the estimates reflect wages only at age 30, which does not take into account increasing skill differentials in earnings with rising age.

Zax and Rees (2002) estimated a series of models of determinants of annual earnings using the Wisconsin Longitudinal Study of Social and Psychological Factors in Aspiration and Attainment, a unique dataset that included a sample of Wisconsin high school graduates who were surveyed at both ages 35 and 53. The overall association at age 35 was 0.75% higher earnings per IQ point. Among graduates at age 53, the associations were approximately twice as large as those observed at age 35, with an overall association of 1.39% per IQ point. This study is considered superior because it allowed for an analysis of the effect of cognitive ability on earnings over the lifespan and included both wages and annual hours of work in its estimate of annual earnings.

Grosse concluded that the analyses by Zax and Rees (2002) and Heckman, Stixrud, and Urzua (2006) imply a total effect of a 1-point difference in IQ scores of 0.8% or 0.9% on earnings for both men and women (average of .85) in their early 30s. However, according to the estimates in Zax and Rees, the overall association with earnings for people in their early 50s is substantially stronger: 1.39% per 1-point difference in IQ scores. Grosse

therefore elected to use the average of the values (.85% and 1.39%= 1.1%). He noted that no perfect estimate of the relation between IQ and earnings exists; findings in any given study depend on the assumptions made by the investigators; and behavioral factors influence earnings at least as much as does cognitive ability (Heckman and Rubinstein, 2001). Because neurotoxins can influence both cognitive and noncognitive ability, economic analyses of the effects of reducing neurotoxin exposures on cognitive ability alone can understate the overall economic benefit.

For our Case 2 estimate, we applied the lower end value of a .85% increase in earnings based on Heckman et al. (Heckman, Stixrud, & Urzua, 2006). For reasons given above, we consider this a lower bound estimate. We did not include the higher value of 1.39% estimated by Zax and Rees (Zax & Rees, 2002). We used the published estimate of discounted lifetime earnings (in 2000 dollars) for a 2-year-old member of the birth cohort (Grosse et al., 2002). This is reasonable since most of the CCCEH cohort was enrolled over a period of several years spanning 2000. Our primary analysis used a 5% discount rate; we have also provided an analysis using a 3% discount rate.

We present two estimates of the economic benefit: Case 1 (ñbest estimateò) is based on the published best estimate (1.1%) for the increase in earnings per IQ point and the best estimate of the increase in IQ per unit decrease in PAH from the CCCEH cohort study; and Case 2 (ñlower estimateò) is based on the lower published value for the increase in earnings per IQ point and the lower estimate of the observed increase in IQ per unit decrease in PAH.

Results

Based on our prior study (F. P. Perera et al., 2009), a one LnPAH unit decrease is associated with a 3 point increase in IQ. Assuming log linearity of dose-response (based on our

data), the effect on IQ of a specified reduction in PAH exposure can be calculated as:

$$\mathrm{IQ}_2 - \mathrm{IQ}_1 = \hat{\beta}\left(\log(PAH_2) - \log(PAH_1)\right) = \hat{\beta}\log\left(\frac{PAH_2}{PAH_1}\right) \text{ where } \beta=-3.$$

The IQ regression model is IQ = alpha + beta*log(PAH) = alpha -3.0*log(PAH). With two levels of PAH and two levels of IQ: IQ_1 = alpha -3.0*log(PAH_1) and IQ_2 = alpha -3.0*log(PAH_2). So:

$$IQ_2 - IQ_1 = -3.0*[\log(PAH_2) - \log(PAH_1)] = -3.0*\log(PAH_2/PAH_1)$$

For a 25% reduction in PAH from 1 to.75 ng/m^3, the best estimate of the gain in IQ is .86 point (-3*log[1/.75]). The lower bound of the effect of PAH on IQ is -0.77 [$\hat{\beta}$+1.96x*se*($\hat{\beta}$), where $\hat{\beta}$=-3, *se*($\hat{\beta}$)=1.14]. Using the lower PAH effect, the gain in IQ corresponding to a 25% reduction in PAH from 1 to.75 ng/m^3 is .22 point (-0.77*log[1/.75]).

We then followed the steps and assumptions of Grosse et al. (Grosse et al., 2002) in estimating the effect of one IQ point on lifetime earnings. For the difference in earnings resulting from a one IQ point difference, Grosse et al. used an estimate of the present value (PV) of future lifetime earnings (2000 dollars) for a 2-year-old child, calculated using a 3% discount rate ($723,300) and also using a 5% discount rate ($353,400) and a 0% discount rate. We have provided results using 5% and 3% discount rates as recommended by an expert panel convened by the U.S. Public Health Service (Gold, Siegel, Russel, & Weinstein, 1996). Our primary analysis (see **Table 1**) was based on the 5% interest rate; in the text we also summarize the results based on the 3% interest rate.

The lifetime economic gain that would be enjoyed by each year's birth cohort as a result of the specified decrease in PAH exposure is given in **Table 1**. For a reduction from 1 to .75 ng/m^3 PAH concentration in air, for each annual cohort of NYC Medicaid births, the Case 1 estimate is $215 million; and the Case 2 estimate is $43 million. The Case 1 estimate

corresponds to a .96% increase in total earnings per person (3,382/353,400; the Case 2 estimate corresponds to a .18% increase in total earnings per person (671/353,400).

With a 3% discount rate, the present value of lifetime earnings was calculated to be $723,300 (Grosse et al., 2002). Using a 3% discount rate, the Case 1 estimate of the benefit per cohort of a 25% reduction in the level of PAH air pollution from 1 to .75 ng/m^3 (in 2000 dollars) is $441 million; the Case 2 estimate is $87 million.

To test the plausibility of our estimated benefit to IQ from a major reduction of ambient PAH concentrations to close to zero, we calculated the increase in IQ from a 75% reduction from 1 to 0.25 ng/m^3 using the formula above. The best estimate was 4.16 points (-3*log 0.25/1). We then added this value to the mean full scale IQ score in the CCCEH cohort of 98.72. The resulting average of 102.88 is comparable to the average for a norm group where the average is 100.

Discussion

This analysis estimates high costs of loss of earnings associated with IQ loss that may be attributed to prenatal PAH exposure for Medicaid births in a single year in NYC--hence potentially large economic gains from the specified modest reduction in ambient PAH concentrations. To the best of our knowledge, this is the first study to estimate the costs of IQ loss associated with PAH exposure and the corresponding benefits of PAH exposure reduction. Given the paucity of data available on the cost of environmentally-related neurodevelopmental effects, we view our findings as a useful departure point for future researchers as well as policymakers, who often need to act in the face of uncertainty.

We have defined our population at risk as one with similar demographic characteristics as our study cohort; i.e., the NYC Medicaid population. However, given that PAH are ubiquitous

in urban environments, benefits will undoubtedly accrue to other groups as well, although their impacts may be smaller than estimated here for this low income population. Moreover, PAH and diesel exposure have been linked to other outcomes, such as various cancers and childhood asthma (Bostrom et al., 2002; Miller et al., 2004), therefore reductions in PAH would be likely to lead to improvements in other health outcomes as well. The annual costs of environmentally-related childhood asthma alone in the U.S. have been estimated at more than $2.0 billion (Landrigan, Schechter, Lipton, Fahs, & Schwartz, 2002). We have not included the potential economic benefits of reducing PAH-related childhood asthma.

While IQ provides the best documented relationship with economic criteria, there are a number of important limitations to the use of IQ as the outcome. These include the difficulty in estimating the impact of cognitive ability on earning potential (Grosse et al., 2002). Further, a loss of 1 IQ point in a disadvantaged population results in a much larger number of individuals added to the developmentally disabled category compared to the same IQ loss in a population of more advantaged individuals; thus expenditures arising from increased demands for remedial education in a disadvantaged community would greatly exceed those in the advantaged community (Weiss, 2000).

The present estimates of the association between prenatal PAH exposure and IQ are based on a peer-reviewed study that controlled for a number of important confounding factors, including measures of the mothers intelligence and the quality of the home caretaking environment (F. P. Perera et al., 2009). A parallel cohort study in Poland reported a similar effect of prenatal PAH on a complementary measure of intelligence at age 5 (Edwards et al., 2010). Related findings from other epidemiological studies discussed above and experimental animal studies of PAH also provide evidence of adverse neurodevelopmental impacts from exposure to PAH (Saunders, Das, Ramesh, Shockley, & Mukherjee, 2006; Saunders, Ramesh, & Shockley, 2002; Saunders, Shockley, & Knuckles, 2003; Wormley, Chirwa, et al., 2004; Wormley, Ramesh, & Hood, 2004). However, although we have found a statistically significant

relationship between PAH exposure and IQ reduction in our cohort, our sample size is limited; and we cannot entirely rule out the possibility of unmeasured confounding.

A further limitation of our analysis is our assumption that women from the NYC Medicaid population face comparable risks from PAH exposure as our cohort. Although the two populations have comparable baseline characteristics, the CCCEH sample excludes smokers and those with other serious medical conditions, so if these factors interact with PAH on risk of IQ loss, our findings may not be readily generalizable to the entire Medicaid population and may underestimate the effect on IQ. In addition, in the absence of city-wide personal air monitoring data we cannot directly ascertain that PAH exposure to the NYC Medicaid population is comparable to that of the CCCEH cohort. However, as discussed above, data from NYCCAS reinforce our selection of the NYC Medicaid population as our population at risk.

Although the Clean Air Act lists several PAH as hazardous air pollutants, there are currently no ambient standards for PAH in the U.S. However, several European countries have set non-mandatory ambient standards or guide values for PAH of 0.1 ng/m^3 and for BaP of .5 ng/m^3 (World Health Organization, 1986). The estimated ambient concentration in NYC of ~1 ng/m^3 is higher than the European guide values.

There are a number of approaches for reducing PAH emissions including fuel efficiency and conservation, innovations in emissions control technology, and use of alternative fuels that emit less PAH. Because interventions pose costs as well as benefits to society, studies such as this suggest the need to factor long- term health benefits into calculations of the societal benefits and costs of these approaches. An assessment of the costs of controlling emissions of PAH from the diverse sources (vehicles, power and industrial plants, residential oil burners, fuel switching etc,) is beyond the scope of this analysis. Moreover, a full cost-benefit analysis for PAH would involve monetizing all other effects of PAH on both health and welfare. The benefits calculated here are relatively modest compared, for example, to the estimated benefits of the EPA mercury and air toxics standards for coal and oil-fired power plant (between $37 and $90

billion using a 3% discount rate and $33 to $81 billion using a 7% discount rate) (EPA, 2011). However, the estimated benefits of that EPA regulation pertain to the entire U.S. population and included reductions in adult morbidity and mortality as well as increases in child IQ. Here we focused only on the single outcome of IQ and we restricted to the low income, Medicaid population of NYC. A somewhat more direct comparison is to the estimate by Grosse et al. of the economic benefits in the entire U.S. population resulting from the reduction in childrenôs exposure to lead over the 12- year period between 1976 and 2002 ($53.8 billion using a 5% discount rate)(Grosse et al., 2002).

In conclusion, this paper suggests significant economic costs from one aspect of reduced cognitive function associated with low level prenatal PAH exposure. The associated impacts are likely to be similar in other urban areas with comparable PAH levels. Our analysis supports policies aimed at decreasing the level of PAH in the ambient air in order to reduce the health and developmental impacts associated with PAH exposure.

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Table 1. Assumptions and Results of Calculations of the Economic Benefit to the 2000 Birth Cohort from a Hypothesized Reduction in PAH Exposure from 1 to .75 ng/m^3

(Adapted from Grosse et al., 2002)

Parameter	Lower estimate (Case 2)	Best estimate (Case 1)
A. Reduction in Ln(PAH) (ng/m^3)	.29[1]	.29[1]
B. IQ Ln(PAH)Slope	.77	3.0
C. Earnings- IQ Slope (%)	.85	1.1
D. Present value of earnings of 2-year-old (in 2000 dollars)(5% discount rate)	353,400	353,400
E. Size of 2-year-old cohort at risk	63,640	63,640
Value of one IQ point (in 2000 dollars) (C x D)	3,004	3,887
Benefit of PAH change from 1 to .75 ng/m^3 in terms of lifetime earnings per individual[2] (in 2000 dollars) (A x B x C x D)	671	3,382
Benefit per cohort (in 2000 dollars) (A x B x C x D x E)	42,687,858	215,232,898

[1]..29=log(1)-log(0.75)

[2] Gain in IQ for a reduction from 1-.75 ng/m^3: Case 1=.86; Case 2=.22 (see text)

CONCLUSION

The dissertation has presented three interrelated original papers providing new evidence supporting a broad, integrated policy to reduce environmental degradation and inequality. The three papers have addressed important research gaps and provided needed evidence to support greater protection of children.