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Testimony before the
Senate Field Hearing on Toxic Chemicals and Children's Health
10-26-10

Introduction

I am Dr. Frederica Perera, Director of the Columbia University Center for Children's Environmental Health (CCCEH), and Professor of Environmental Health Sciences at the Columbia University Mailman School of Public Health in Manhattan.

CCCEH was founded in 1998 with joint funding from the National Institute of Environmental Health Sciences and the US EPA with the mission to improve the health and development of children by identifying environmental toxicants as well as genetic, nutritional, and socioeconomic factors that increase their risk of disease. In 1998 we knew that there were ever-increasing human exposures to environmental toxicants and that rates of neurodevelopmental disorders and chronic illnesses such as childhood asthma and cancer were on the rise. While it was clear that these diseases had multiple causes, environmental exposures such as lead, mercury and polychlorinated biphenyls were known to contribute. It had also become evident over the previous decades that the placenta does not adequately protect the fetus from toxicants and that, due to their rapid development and immature defense systems, the developing fetus, infant and child are especially susceptible to environmental toxicants (Perera et al., 2006). Moreover, there was emerging evidence that the *in utero* environment could help shape health over the lifecourse. This knowledge and the fact that, unlike genetic susceptibility factors, environmental exposures are by nature preventable, prompted us to focus on the relation between early-life exposures to common environmental pollutants (air pollutants, pesticides and other chemicals) and neurodevelopmental disorders, asthma, indicators of cancer risk, and more recently, obesity and metabolic disorders in children.

In my testimony, I will focus on endocrine disrupting chemicals and neurodevelopmental disorders, noting that an estimated 5-17% of United States children have been diagnosed with a learning or attention disorder (Centers for Disease Control and Prevention 2005).

Research at the Columbia Center for Children's Environmental Health

At CCCEH, since 1998 we have conducted international studies of cohorts of mothers and children followed from pregnancy - two of which are in New York City (NYC)- and others in Poland and China. In one ongoing study begun in 1998 the participants are African American and Dominican women and children who live in Northern Manhattan and the South Bronx ("Northern Manhattan Cohort"). The other study is our World Trade Center Cohort Study in which the participants are a racially diverse (Caucasian, Asian and African American) group of women from the NYC greater metropolitan area who were pregnant on September 11, 2001 and their children. The NYC cohorts have been followed from enrollment during pregnancy for 6-12 years and follow-up in the Northern Manhattan Study is ongoing. We have conducted repeat interviews and personal air monitoring assessments to gain information on the pollutants and chemicals our study participants were exposed to during pregnancy and later in childhood. We have also measured biomarkers of exposure, preclinical effect, and susceptibility in small samples of blood and/or urine collected from the mothers and children over the course of the

study. And we have conducted clinical assessments of children's development and health as they grew older.

Today I will share with you our results on just four of the chemicals our Center investigators have studied: phthalates, bisphenol A (BPA), and polybrominated diphenyl ethers (PBDEs). Phthalates are used in production of plastics to increase flexibility of the material. BPA is used to make plastic baby and water bottles and medical and dental devices as well as coatings on the inside of food and beverage cans. PBDEs are a group of flame retardant chemicals applied to home furnishings, polyurethane foams, textiles, electronics, and many other products. Chlorpyrifos is an organophoshate insecticide which, prior to its phase-out for residential use in 2001, was commonly used within households to control pests such as cockroaches. Chlorpyrifos is still utilized for agricultural purposes.

All of these chemicals are capable of disrupting the endocrine system (Roy 2009; Heudorf et al. 2007; Oehlmann 2008; Charboneau 2008). Endocrine disruptors are substances that interfere with hormone production and/ or hormonal activity. Endocrine disruption is an important area of concern for health scientists because we are becoming increasingly aware that very low exposures to endocrine disruptors can result in altered hormone regulation and activity. We are still learning about the health implications of this mechanism for development and reproduction, but the fact that these chemicals can alter natural hormonal pathways at such low exposure levels is a real concern.

Evidence of widespread exposure

Our data confirm that these chemicals are ubiquitous in the environment. in the Northern Manhattan cohort, we detected phthalates in 85–100% of air and urine samples from pregnant women (Adibi et al. 2008). We detected BPA in the urine of 94% of pregnant women, 97% of 3 year olds and 100% of 5 year olds, with a wide range of concentrations (unpublished data).

We identified at least one PBDE in 81% of cord blood samples from newborns in the World Trade Center cohort (Herbstman et al. 2010). PBDE concentrations were unrelated to proximity to the WTC, indicating widespread "background" exposure. Nor is widespread exposure to these chemicals specific to New Yorkers: the Centers for Disease Control's 2009 National Report on Human Exposure to Environmental Chemicals shows that individuals across the country are commonly exposed to these chemicals (CDC, 2009).

The personal air monitoring data from our Northern Manhattan cohort revealed that 100% of the pregnant women in the study were exposed to inhalable chlorpyrifos (Whyatt et al. 2003). Chlorpyrifos was detected in 71% of umbilical cord specimens within the cohort (Whyatt et al., 2003).

Associations between chemical exposures and developmental outcomes

In our Northern Manhattan cohort, phthalate exposure was associated with shortened gestational age (Whyatt et al. 2009a). This is of concern as even slightly shortened gestation has been associated with health problems later in life, ranging from poor school performance (Kirkegaard et al. 2006) to depressive symptoms (Raikkonen et al. 2007). Follow-up in our cohort is ongoing. A study by our colleagues at Mount Sinai found that prenatal phthalate exposure was associated with adverse effects on behavior and executive functioning at 4-9 years of age (Engel et el., 2010).

We are currently analyzing our cohort data regarding the association between prenatal concentrations of BPA and neurobehavioral outcomes in our children. A recent study by other

investigators found that prenatal BPA concentrations were associated with externalizing behaviors in 2 year old girls (Braun et al. 2009), consistent with several prior laboratory based studies that reported reduced sexual dimorphism in the brain structure and altered behavior of offspring, such as greater anxiety- like behavior and hyperactivity (McCarthy 2008) (Ryan and Vandenbergh 2006) (Mizuo et al. 2004).

In our World Trade Center cohort, we found that children exposed to higher levels of PBDEs had significantly impaired psychomotor and mental development as well as lowered IQ for virtually all neurodevelopment assessments conducted between 1-6 years of age (Herbstman et al. 2010). Although these findings are among the first to link PBDE exposure with adverse neurodevelopmental effects in humans, our results are consistent with laboratory-based studies which link PBDE exposure to learning and memory deficits (Costa and Giordano 2007).

Chlorpyrifos- legislative success in progress

As a final example of our research, CCCEH showed that maternal exposure to chlorpyrifos is associated with decreased birth weight and birth length (Whyatt et al., 2005). Additionally, when exposed to high levels of chlorpyrifos *in utero*, these children are more likely to have psychomotor and mental development delays by age 3, as well as attention deficit and hyperactivity problems (Rauh et al. 2006). Importantly, our data show that air and cord blood measures of chlorpyrifos decreased significantly following the Environmental Protection Agency's residential ban of this insecticide in 2001, testifying to the immediate benefit of regulatory intervention (Whyatt et al. 2009b).

Concluding Remarks

I have just shared with you some of the research of our Center and from our colleagues in the field that show the link between fetal and child exposures to phthalates, BPA, and PBDEs, and adverse developmental and neurodevelopment effects. The example of chlorpyrifos demonstrates the benefit of reducing a toxic exposure to pregnant women and the developing fetus.

However, a preventive approach is clearly needed, as illustrated by the case of lead. Lead was originally introduced to gasoline as an anti-knocking agent in the 1920s; but It was not until the early 1970s that the Environmental Protection Agency's regulation limiting lead quantity in gasoline was enforced, based on accumulating knowledge at the time that lead is a potent neurotoxin (EPA 1999). Lead was also widely used in paint and it was not until 1977 that the US Consumer Product Safety Commission banned lead paint. For 50 years, therefore, exposure to lead was widespread, with significant adverse neurologic impacts on children. The environmentally attributable economic cost of lead poisoning in New York State is estimated to be $3.66 billion in 2000 alone (Trasande et al. 2005). Since lead exposure reduction in the 1970s, there has been an estimated $56,000 economic benefit *per child* in the United States based on removal of environmental lead exposure alone (Grosse et al. 2002).These figures do not, of course, reflect the unquantifiable cost to the lives of children who have suffered lead poisoning. The case of lead reminds us strongly of the need for testing of chemicals before they are released to the environment and the timely regulation of those shown to be harmful.

Of course uncertainties in data and inconsistencies across studies do exist, due in part to different study designs and populations studied. Questions remain even today as to the safe level of lead (Lanphear et al., 2005). However, given the widespread exposure to chemicals such as those I have discussed, these uncertainties do not outweigh the need for a preventative

approach to children's health. The public health and economic benefits of prevention are clearly great. Our data and those of many others support a preventative chemical policy to protect our youngest and most susceptible population.

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