Targeted Research Area: Environmental Toxicants

General Information on Environmental Toxicants

- **Prevalence and incidence of diseases associated with environmental toxicants:**
  - Reported rates of asthma, developmental disorders, and cancer in children have increased in the past decades. Although improved detection and reporting have contributed to these observed increases, environmental factors play a role. Reported rates of ADHD, learning disabilities, and autism have markedly increased in the U.S. in the last decade.[41] Approximately 17% (12 million) of U.S. children (<18 years of age) have one or more developmental disabilities; 3-6% are affected by ADHD; 5-10% are affected by learning disabilities. Incidence of autism may be as high as 2/1,000.
  - Rates of these diseases are disproportionately high in underserved, minority populations in low-income communities.[42]
  - As many as 28% of all neurodevelopmental disabilities in children are of environmental origin. There has been increasing incidence in conditions thought to be caused by endocrine disruptors. There has been increasing incidence in pediatric cancers; glioma, the second most common malignancy in children, has increased in incidence by close to 40% since 1972.[43]
- **Mortality from environmental toxicants:** Mortality rates vary depending on the toxicant exposure and associated disease outcome.
- **Disease severity/disease burden:** Disease severity or burden varies depending on the disease outcome.
- **Cost to individual/family/society/healthcare system:** Cost varies depending on the disease outcome.
- **Frequency/load of exposure to environmental toxicants:**
  - Children's exposure and susceptibility to environmental toxicants vary with their developmental stage.[44]
  - The frequency of exposure to environmental toxicants is dependent on the physiologic characteristics, behavioral patterns, and developmental stages of children.[45]
  - An estimated 25,000 children are poisoned by pesticides each year.[46]

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41 Perera FP, Illman SM, Kinney PL, Whyatt RM, Kelvin EA, Shepard P, et al. The challenge of preventing environmentally related disease in young children: community-based research in New York City. Environmental Health Perspectives 2002;110(2):197-204.

42 Ibid.

43 Landrigan PJ. Children's environmental health. Lessons from the past and prospects for the future. Pediatric Clinics of North America 2001;48(5):1319-30.

44 Gitterman BA, Bearer CF. A developmental approach to pediatric environmental health. Pediatric Clinics of North America 2001;48(5):1071-83.

45 Hubal EAC, Sheldon LS, Burke JM, McCurdy TR, Berry MR, Rigas ML, et al. Children's exposure assessment: a review of factors influencing children's exposure, and the data available to characterize and assess that exposure. Environmental Health Perspectives 2000; 108(6):475-86.

46 Centers for Disease Control and Prevention. *The Children's Environmental Health Report Card.* Available at: http://www.cdc.gov/nceh/asthma_old/factsheets/reportcard.htm

- **Special populations:** This information was not readily available to The Lewin Group.

Hypotheses 12 - 14, described on the following pages, are associated with the Environmental Toxicants targeted research area.

Hypothesis #12: Exposure to contaminants in water, such as chlorine disinfection byproducts, can lead to adverse birth outcomes such as neural tube defects, low birth weight, and spontaneous abortions.

General Information Related to Hypothesis #12

- **Frequency/load of exposure to contaminants in water:**
  - 85% of all homes in the U.S. receive their water from public water systems. Most of these systems use chlorine for disinfection, leading to exposure to potentially harmful chlorination disinfection by-products.[47]
  - Exposure to disinfection byproducts (DBPs) is likely to be misclassified due to a variety of factors, including variability in water consumption, seasonal variability in DBP formation, and exposure to other sources of DBPs.[48]
- **Findings from recent research (targeted search):** Information reported in the following two studies contributed to the above-mentioned hypothesis.

Study #1: Bove F, Shim Y, Zeitz P. Drinking water contaminants and adverse pregnancy outcomes: a review. Environmental Health Perspectives 2002;110:61-74.

Study #1 hypothesis being tested: Drinking water contaminants (e.g., chlorination disinfection byproducts) are associated with adverse pregnancy outcomes.

Study #1 findings: Moderate evidence from studies of trihalomethanes, a type of chlorination disinfection by-product present in drinking water, have shown an association with small for gestational age (SGA) infants, neural tube defects, and spontaneous abortions. The authors suggest the association between water contaminants, and chlorinated solvents in particular, and adverse birth outcomes be included in a national longitudinal study tracking the prenatal through adolescent periods.

Study #2: Zender R, Bachand AM, Reif JS. Exposure to tap water during pregnancy. Journal of Exposure Analysis and Environmental Epidemiology 2001;11(3):224-30.

Study #2 hypothesis being tested: Exposure to disinfection byproducts (DBP), which is associated with adverse reproductive outcomes, is likely to be misclassified. (Please note: this article focuses on the exposure, rather than the disease area.)

Study #2 findings: Misclassification of exposure in studies of DBPs and reproductive outcomes is likely to arise from several sources including residential mobility during pregnancy, use of private wells rather than municipal system, individual variability in daily water consumption, seasonal variability in DBP formation and spatial

[47] Bove F, Shim Y, Zeitz P. Drinking water contaminants and adverse pregnancy outcomes: a review. Environmental Health Perspectives 2002;110:61-74.

[48] Zender R, Bachand AM, Reif JS. Exposure to tap water during pregnancy. Journal of Exposure Analysis and Environmental Epidemiology 2001;11(3):224-30.

concentrations of DBPs within the distribution system. In addition, failure to account for dermal and inhalation exposures to DBPs is likely to lead to an underestimate of total exposure. Study results heighten concern about DBP exposure estimates as individual differences in water consumption must be taken into account when assessing exposure to DBPs.

Hypothesis #13: Exposure to environmental toxicants, such as air pollutants and DEHP (di-2-ethylhexyl phthalate), can affect various stages of child development, from intrauterine to postnatal development.

General Information Related to Hypothesis #13

- **Frequency/load of exposure to DEHP:** The average total daily individual ambient exposure to DEHP in the U.S. is estimated to be 0.27 mg per day, excluding workplace air exposures, and indoor air exposures from off-gassing of building materials. Daily exposures in the medical setting may be three times the magnitude of exposure in the general population. Medical devices contain 30-40% DEHP by weight. The degree of leaching from a medical device can be as much as 10-15% of the available DEHP in the device. Newborns receive among the highest doses of DEHP from blood transfusions, extracorporeal membrane oxygenation, and respiratory therapy. DEHP can also cross the placenta, exposing the fetus.[49]
- **Findings from recent research (targeted search):** Information reported in the following four studies contributed to the above-mentioned hypothesis.

Study #1: Pereira LAA, Loomis D, Conceicao GMS, Braga ALF, Arcas RM, Kishi HS, et al. Association between air pollution and intrauterine mortality in Sao Paulo, Brazil. Environmental Health Perspectives 1998;106(6):325-329.

Study #1 hypothesis being tested: There is an association between intrauterine mortality and air pollution.

Study #1 findings: The study showed that the association was strong between intrauterine mortality and air pollution for NO_2, but less for SO_2 and CO. The association was stronger when all three pollutants were considered together. The study results showed a significant association between air pollution and intrauterine mortality in San Paulo for the period January 1991 to December 1992. The authors state that there have been few studies on the susceptibility to air pollution and the possible effects of air pollution on fetuses.

Study #2: Gitterman BA, Bearer CF. A developmental approach to pediatric environmental health. Pediatric Clinics of North America 2001;48(5):1071-83.

Study #2 hypothesis being tested: Children's exposure and susceptibility to environmental toxicants vary with their developmental stage.

Study #2 findings: There are differences in exposures, pathways of absorption, tissue distribution, ability to bio-transform or eliminate chemicals from the body, and responses to chemical and radiation. The differences vary with each developmental

[49] Tickner JA, Schettler T, Guidotti T, McCally M, Rossi M. Health risks posed by use of Di-2-ethylhexyl phthalate (DEHP) in PVC medical devices: a critical review. American Journal of Industrial Medicine 2001;39(1):100-11.

stage of the child. Children respond differently to environmental toxicants than adults and thus cannot be considered "little adults" in the field of environmental medicine.

Study #3: Tickner JA, Schettler T, Guidotti T, McCally M, Rossi M. Health risks posed by use of di-2-ethylhexyl phthalate (DEHP) in PVC medical devices: a critical review. American Journal of Industrial Medicine 2001;39(1):100-11.

Study #3 hypothesis being tested: Di-ethylhexyl phthalate (DEHP) exposure from medical care materials may have adverse health effects in certain groups of patients, particularly developing fetuses and neonates.

Study #3 findings: Sufficient toxicological data are readily available to cause concern about exposure to fetus, neonate, infant, child, or chronically ill. Due to the variability of toxicity of DEHP in multiple organs, the variability in human exposure and susceptibility to effects and uncertainties in extrapolating animal data to humans, estimates of human risk or safe levels of exposure cannot be established at this time. Epidemiological studies of DEHP-exposed humans are not available. The authors note that due to limitations of current data, further research should be conducted to better understand and characterize DEHP.

Study #4: Hubal EAC, Sheldon LS, Burke JM, McCurdy TR, Berry MR, Rigas ML, et al. Children's exposure assessment: a review of factors influencing children's exposure, and the data available to characterize and assess that exposure. Environmental Health Perspectives 2000; 108(6):475-86.

Study #4 hypothesis being tested: Physiologic characteristics, physical activities, dietary habits, sex, socioeconomic status (SES) and race/ethnicity of children all influence children's exposures to environmental contaminants. (Please note: this article focuses on the exposure, rather than the disease area.)

Study #4 findings: Physiologic characteristics affect a child's rate of contact and exposure by affecting exposure uptake. Infants have a surface area-to-body ratio twice as great than that of adults. Diets of infants and children are usually very limited and may increase their exposure to environmental contaminants such as pesticide residues in fruit. Gender affects activity levels and behavior of children and may account for variance in type of exposures encountered. The authors state that data are insufficient to characterize a relationship between SES, ethnicity/race, age and environmental exposure. Improvements need to be made to data collection efforts. The authors call for more research on the identification of appropriate benchmarks for categorizing children in exposure assessments (e.g., according to when developmental changes occur), development and improvement of methods for monitoring exposures and activities, and collection of physical activity data for children to assess exposure by all routes.

Hypothesis #14: Exposure to environmental toxicants such as pesticides (e.g., organophosphates) can play a causal role in childhood diseases ranging from asthma to neurological disorders.

General Information Related to Hypothesis #14

- **Exposure to environmental toxicants:**
  - 34.5 million kg (76 million lbs) of active pesticide ingredients were used in home and garden settings, according to most recent EPA estimate (1997).[50]
  - One report suggested that during the period of 1997-99, organophosphates was one class of pesticide that most likely caused illness or death in U.S. children. Exposures to this pesticide totaled 40,090 over this time period. Moderate or severe morbidity from exposure to organophosphates totaled 1,994 patients from 1997-99. Twenty-one deaths were related to exposure to this class of pesticide over the same period of time.[51]
  - Children are at risk for exposure to 2,800 high-production-volume (HPV) chemicals that are produced in quantities of more than 1 million tons per year. These HPV chemicals are distributed widely in the environment. Only 43% of HPV chemicals have been tested for their potential to cause toxicity; fewer than 20% have been tested for their ability to interfere in child development.[52]
- **Findings from recent research (targeted search):** Information reported in the following study contributed to the above-mentioned hypothesis.

Study #1: Perera FP, Illman SM, Kinney PL, Whyatt RM, Kelvin EA, Shepard P, et al. The challenge of preventing environmentally related disease in young children: community-based research in New York City. Environmental Health Perspectives 2002;110(2):197-204.
(Note: This study is also cited under the research areas of asthma, childhood cancer, and neurodevelopmental disorders.)

Study #1 Hypothesis being tested: Prenatal and postnatal exposure to environmental toxicants can lead to respiratory disease, impaired neurological development, genetic damage, and increased risk of cancer.

Study #1 Findings: Environmental toxicants can modify the formation and maturation of the lungs. In utero sensitization to specific allergens can occur independently of maternal sensitization, putting children at higher risk for asthma. Neurochemical and behavioral effects arise from exposure to toxicants during critical windows of fetal development. Fetuses also clear toxicants less efficiently than adults and are more vulnerable to genetic damage and subsequent risk of cancer. Nutritional deficits in maternal diet have been linked to development of asthma in the child. Gene-environment interactions and psychosocial factors can also make a fetus or newborn

[50] Reigart JR, Roberts JR. Pesticides in children. Pediatric Clinics of North America 2001;46(5):1185-98.
[51] Ibid.
[52] Landrigan PJ. Children's environmental health. Lessons from the past and prospects for the future. Pediatric Clinics of North America 2001;48(5):1319-30.

more susceptible to disease. Some studies suggest that women who live in violent, crime-ridden neighborhoods experience pregnancy complications and adverse birth outcomes. Prenatal and postnatal exposure to environmental toxicants can lead to respiratory disease, impaired neurological development, genetic damage, and increased risk of cancer. Nutrition, gene-environment interaction, and psychosocial stressors are cofactors that compound the susceptibility of the fetus and newborn.