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ENVIRONMENTAL CHEMICALS IN BREAST MILK & INFANT FORMULA AND THE RELATIONSHIP TO INFANT/CHILD HEALTH

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Introduction:

Infancy and other early stages of life are the foundation for a child's growth, maturation, and overall health status throughout the rest of childhood and adulthood, therefore it is important to scientifically understand the optimal environment and diet for a child's first months. Recent reviews on the health benefits of breastfeeding affirm that breastfeeding confers numerous benefits to infants compared to formula feeding (AAP 2012; Ip et al. 2007). As recommended by the American Academy of Pediatrics (AAP) and the World Health Organization (WHO), infants should be exclusively breastfed for the first 6 months of life (AAP 2012; Kramer and Kakuma 2012). There is strong evidence supporting the association of breastfeeding with a reduced risk of acute otitis media, severe lower respiratory infections, non-specific gastroenteritis, atopic dermatitis, asthma, obesity, type 1 and 2 diabetes, sudden infant death syndrome (SIDS), and childhood leukemia, as well as necrotizing enterocolitis and neurodevelopmental problems in pre-term infants (AAP 2012; Ip et al. 2007; Victora et al. 2016).

At the same time, it has been well documented that breastmilk contains various environmental chemicals of which breastfed infants are exposed to. Because the infancy stage of life lays the foundation for lifelong health, it is essential that the scientific community be able to accurately determine levels and types of environmental chemical exposures during this stage and assess related health outcomes in infancy and childhood (Lehmann et al. 2014). A major environmental chemical exposure pathway for infants is via diet, either from breastfeeding or formula feeding. Perhaps the earliest attempt to measure environmental chemicals in breast milk was a study by Laug et al. (1951) who reported measurements of DDT. For formula-fed infants, the data on exposure to environmental chemicals via diet is much sparser.

Since the time of that publication, the number of reports on concentrations of environmental chemicals in breast milk has grown rapidly, with publications now available for a large number of chemicals from countries around the globe, though the U.S. lacks any population-representative sampling. In terms of environmental chemicals in breast milk and infant and child health outcomes, some of the earliest epidemiology studies were published in the late 1980's, and the literature has expanded since that time. In contrast, environmental chemicals in infant formula and associated health outcomes in infants and children have not garnered the same attention.

In this presentation, we will begin with an overview of the definition of environmental chemicals as they pertain to breast milk and infant formula, the types and levels of environmental chemicals found in these sources of infant nutrition, and levels in breastfed infants. As levels of chemicals are likely to have geographic variations, we are principally interested in assessing exposures and outcomes in the US. Where informative, we draw on the literature from other developed countries and, in some instances, from developing countries. We will discuss a critical assessment of the epidemiological literature on exposures via breastfeeding and health outcomes. Lastly, we will describe advances in risk assessment approaches to understanding the potential for effects from environmental chemicals in breast milk and formula, and close with a discussion of research needs and conclusions.

Materials and Methods:

The electronic data sources PubMed and EMBASE were used to conduct the initial literature search. Using keywords "breast milk", "PBDE", "DDT", "DDE", "organochlorine", "pesticide", "dioxin", "furan", "PCB", "lead", "mercury", "growth", "development", "neurodevelopment", "infant health", "PFOS", "perfluorinated", "humans", "chemicals," as well as various combinations of these keywords, we identified articles that investigated the health effects associated with environmental chemicals in breast milk.

Secondary references of retrieved articles were reviewed to identify publications not captured by the initial electronic search. The search and selection of relevant studies was conducted by one study author. The criteria for inclusion in the review were as follows: (1) Studies of human populations with at least

one measurement of chemical(s) levels in breast milk; (2) Outcomes assessed in infant/child population (studies that relied on risk calculations in the absence of actual observations of health outcomes were not included); (3) Associations between chemical exposure and outcomes were assessed by the publication authors; (4) Study populations exposed at background levels (poisonings/accidental exposure events are not considered here); and (5) English-language publications present in the peer-reviewed literature prior to 1 November 2014 (end of literature search).
Each study that met the inclusion criteria was examined, and the data from each study were tabulated. Information extracted from each study for the purposes of this review included the following: (1) Description of the study population (size, composition, source, and location); (2) Study design (cohort, cross-sectional, case-control, or other); (3) Chemical exposure categorization (number of samples, and the type of variable [e.g. ordinal, binary, or continuous] used in the analysis); (4) Outcomes; (5) Statistical approach and covariates included in the model; (6) Results (original text summaries of results were reproduced verbatim or results were paraphrased); and (7) Description of study-specific chemical levels. For this review, regardless of the interpretation of the study authors, we considered any measures of environmental chemicals in milk to be measures of postnatal exposure relevant for understanding associations between chemicals in breast milk and infant formula, and health outcomes. Two authors of this paper reviewed each study. Differences in assessment for any item were discussed until consensus was achieved.

Results and Discussion:
Organochlorine chemicals: Associations between organochlorine chemicals in breast milk and infant and child health outcomes have been studied fairly extensively in several cohorts in multiple countries; some of these cohorts were followed for several years. We will discuss four cohorts in the US (two in North Carolina, one in New York, and one in Michigan) that assessed associations between DDT, DDE and/or PCBs in breast milk and health outcomes in infants and children. Along with several cohorts in Europe, Canada, Asia, and the Caribbean provide additional relevant information on these chemicals as well as for PCDDs/Fs and organochlorine pesticides. Three cohorts in the Netherlands and Germany have been reviewed previously (LaKind et al. 2008a), and descriptions of these cohorts are largely drawn from that review.

Flame Retardants: We will discuss the six epidemiologic studies on background exposures to flame retardants in breast milk and infant health that were identified. As noted by LaKind et al. (2014a), "A critical and, perhaps the only inarguable, property of a causal association is temporality, meaning that a claim of causation must be supported by an observation of the putative causal exposure preceding the outcome…"; as there is conflicting evidence regarding whether or to what degree concentrations in breast milk change over the course of lactation (LaKind et al. 2001, 2009a; Hooper et al. 2007), it cannot be assumed that relevant exposures preceded effect.

Heavy Metals: Research on heavy metals in breast milk and health outcomes has focused on lead, cadmium, methyl/ethylmercury and aluminum. We will provide a brief overview of the literature here but also note that the population exposures described are unlikely to be generalizable to the US population. For example, many of the publications involve cohorts living in close proximity to smelters/kilns in Amazonian Brazil, consuming diets rich in fish from contaminated rivers, and receiving vaccinations that are still preserved with ethylmercury (thimerosal).

Phthalates and PFCs: We will discuss one study on phthalates and one study on PFCs in breast milk and infant health outcomes were identified. Danish/Finnish cohort: Main et al. (2006) investigated whether breast milk levels of phthalate monoesters were associated with a postnatal surge of reproductive hormones in newborn boys from 1997 to 2001. In the study by Wohlfahrt-Veje et al. (2014), described above in the section on PBDEs, breast milk samples (N=418; collected between 1-3 months postpartum) were randomly collected among samples with sufficient volume for measuring PFOA and PFOS.

In this comprehensive examination of the environmental epidemiology literature on associations between environmental chemicals in breast milk and infant/child health outcomes, we sought to identify aspects of the literature that, taken together, would inform public health discussions about this critical life stage. While a relatively large number of cohorts have been studied, and many studies reported no associations between exposure and outcome, the number of chemicals that have been addressed by the body of

research is relatively small. Further, the number of strong studies that have replicated findings from earlier studies is extremely limited.

This critical assessment of the available information on – and approaches to – understanding the concentrations of environmental chemicals in breast milk and infant formula and what those concentrations might mean for infant and child health has highlighted many important shortcomings in the current literature. Additional research in these areas would strengthen our ability to estimate infant dietary exposures to environmental chemicals. These improved exposure estimates would increase our confidence in future epidemiological research results and in estimates of potential for health effects or reductions in health benefits associated with early life diets. Research needs include properly powered studies, implementation of robust exposure assessment methods, adequate recruitment of study participants from the high and low ends of the exposure distributions, and a focus on exposure assessments that include an exposomic approach, as opposed to continuing to focus on one or a few chemicals in a particular study

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