ESTIMATING INFANT BODY BURDENS OF DIOXIN FROM BREAST MILK IN THE US: WHAT WE KNOW, WHAT WE NEED TO LEARN

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Introduction

The importance of breastfeeding in the healthy development and well-being of infants is well recognized.[1] There are, however, a number of factors that may prevent women from initially breastfeeding or breastfeeding for longer periods of time, including the fear of environmental contaminants in their milk. A clear picture of ranges of doses of breast milk contaminants experienced by nursing infants in North America has not yet been described, resulting in a significant gap in our understanding of potential health risks to infants from those contaminants. Although point estimates of infant doses of environmental contaminants from breast feeding appear in published literature, these estimates do not take into account the wide variability in exposures, and therefore, the large range of potential risks experience by nursing infants. There is a critical need to better understand the range of exposures a breastfeeding infant may experience in order to develop more accurate characterizations of the risks and benefits to breastfeeding infants as compared to other feeding methods, including infant formula and solid foods.

This research expands on the current state of understanding of risks associated with breast milk contaminant exposure by characterizing distributions and time-dependency of dose for a persistent contaminant commonly detected in human milk, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). (The methodology is also applicable to other lipophilic chemicals). We describe the development of estimates of ranges of TCDD body burdens in nursing infants in North America.[2] These body burdens do not reflect exposure to TCDD from non-nursing routes such as other dietary sources or placental transfer. The model does not completely eliminate uncertainty in exposure estimates, particularly since certain of the input parameters have been poorly characterized. The extant data on two of these parameters (concentrations of chemicals in breast milk from the US and elimination kinetics during lactation) is reviewed.

Methods and Materials

The following equation was used to estimate TCDD body burden from birth to two years of age:

$$BBTCDD(z) = \frac{\left[\sum_{t=1}^{y} CTCDD(0) \times e^{-k(dep)(t)} \times IR \times p\ milk \times A \times e^{-k(\lambda)(y-t+1)}\right] \times e^{-k(\lambda)(z-y)}}{BW(z)}$$

Where:

$BB_{TCDD(z)}$	=	TCDD body burden at the end of monthly time period (z) (ng TCDD/kg body weight)
$C_{TCDD(0)}$	=	TCDD whole breast milk concentration at time = 0 post partum (ng TCDD/kg milk)
k(dep)	=	TCDD mother's milk depuration rate constant (1/month)
t	=	Time (months)
IR	=	Infant milk ingestion rate (ml milk/month)
ρ_{milk}	=	Density of whole breast milk (kg milk/ml milk)
A	=	Absorption of TCDD in infant (unitless)
$k(\lambda)$	=	TCDD nonmetabolic decay constant in infant (1/month)
y	=	Duration of breastfeeding, or z if z < time at which breastfeeding ceases (months)
z	=	Duration of time period of interest (months)
$BW_{(z)}$	=	Infant body weight at time = z (kg body weight)

The equation was solved probabilistically in order to derive a dose distribution for five nursing durations: 3, 6, 9, and 12 months of breast feeding and a randomly simulated duration of breastfeeding based on national statistics describing the fraction of mothers breastfeeding for specific lengths of time post-partum. The simulation was performed using @RISK. Three categories of input variables were used: chemical, nursing, and infant variables (Table 1).

Results and Discussion

The modeling results demonstrated that the TCDD body burden of North American breastfed infants is expected to rise rapidly from birth to three months of age with a 6-month nursing duration exposure scenario. TCDD body burden is expected to peak at about 5 months of age. A sharp decrease in body burden follows the cessation of breastfeeding. At 24 months post-partum, infant body burden estimates are less than 0.2 ng/kg. Similar trends were observed with other nursing duration scenarios.[2] Of note is that even for infants breastfed for the first 12 months of life, TCDD body burden is expected to peak at the age of approximately 5 months (Figure 1). The change in infant body burdens over time is significant; if one accounts for depuration and half-life, then previous infant body burden estimates which examine daily dose to nursing infants based on one early measure of chemical levels in breast milk would be overly conservative (i.e., body burden predictions would be too high). This research shows that while daily doses of TCDD may exceed adult daily doses (1 to 3 pg TEQ/kg-day[4]), incremental body burdens per unit weight do not approach that of adult body burdens, and body burdens post weaning quickly decline.

Uncertainties in the model results derive from limitations of the data. Insufficient information on depuration is available to confidently describe the range of values for this parameter.[3] Similar limitations exist regarding the reported reduced half-life of lipophilic chemicals in infants. A major limitation is the sparse extant data on representative levels of TCDD and other chemicals in breast milk in the U.S..[3] Considering both the levels of chemicals in breast milk from the US and the depuration during lactation, shortcomings of available studies include: (i) variable sampling and analysis protocols, (ii) incomplete reporting (e.g., sampling methods), (iii) non-representative sampling (geographical, parity, age), (iv) duration of sampling, (v) small populations, and (vi) number and types of chemicals in analysis (e.g., PBDEs). These limitations restrict our ability to predict infant body burdens. A carefully planned and executed program of nation-wide breast milk sampling is critical for (i) performing exposure assessments without reliance on default assumptions or on the small, extant database, and (ii) providing information on trends in breast milk contaminant levels, which indicates whether controls on sources of contaminants are effective. Without this type of information, we will be unable to provide a scientifically-based and consistent message to interested communities (e.g., doctors, nurses, lactation specialists, and new mothers) on benefits and risks of breast feeding in the US. [3]

Despite the uncertainties inherent in modeling incremental body burdens of chemicals from nursing, the following conclusions can be made:

1. Estimating infant body burdens of lipophilic chemicals from breastfeeding using point estimates results in overly conservative estimates of the contribution of breastfeeding to long-term body burdens of those chemicals in children and would perhaps unnecessarily cause concern to nursing mothers. To develop reliable estimates of incremental body burden from nursing, depuration via lactation and half-life in the infant should be considered.
2. Infant body burdens of lipophilic chemicals like TCDD increase rapidly at the start of lactation, but decrease after about 5 months (even if nursing continues); by two years post partum, incremental body burdens have decreased substantially. Thus, comparison of these body burdens with values such as cancer potency factors, which are based on long-term exposures, may not be appropriate. This presents a challenge to improve our understanding of the implications of "...short periods of high exposure to dioxins on the neurological, immune system, reproductive system, endocrinological and intellectual development of such infants".[5]
3. Increased sampling of breast milk is necessary to provide a better basis for characterizing the levels of chemicals in breast milk in the U.S.; a sampling and analysis program on breast milk from the U.S. should be initiated. This type of program would enable the development of a scientifically-based and consistent message on the risks and benefits of breast feeding.
4. Because of the significant advantages to breastfeeding, including protection against infection, and because breastfeeding does not necessarily lead to significantly increased long-term infant body burdens, breastfeeding should be encouraged and promoted. The identification and control of sources of environmental contaminants should continue in order to make human milk as safe as possible.

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Table 1. Model input variables and values used in the analysis of infant body burdens of TCDD and DDE.

Model Input Variable	Values Utilized in Model
Breast milk concentration of TCDD (whole milk basis)[6]	Log mean = -1.08, Log S.D. = 0.21
Maternal depuration rate	50% depuration over a 6-month period of nursing
Breast milk consumed[7]	*800 ml/day*
Percent lipid in breast milk[8]	Mean = 3.57 g/100 ml, S.D. = 0.82 g/100 ml
Density of whole breast milk[9]	1.031 g/ml
Absorption of TCDD by infant[10]	95 percent
Half life of TCDD[11]	0.42 years
Infant body weight[12,13]	Monthly means/standard deviations for breastfed boys/girls

Figure 1. Incremental TCDD body burden in infants breastfed for 12 months post-partum