PREDICTORS OF SERUM DIOXINS AND PCBS IN A RUSSIAN COHORT OF BOYS

Burns Jane S[1], Williams Paige L[2], Sergeyev Oleg[3,4], Korrick Susan[1,5], Lee Mary M[6], Revich Boris[7], Altshul Larisa[1], Turner Wayman E[8], Patterson Donald G Jr[8], Saharov Igor[9], Hauser Russ[1]

[1]Department of Environmental Health, Harvard School of Public Health, Boston, MA, USA [2]Department of Biostatistics, Harvard School of Public Health, Boston, MA, USA [3]Samara State Medical University, Department of Physical Education and Health, Samara, Russia [4]Chapaevsk Medical Association, Chapaevsk, Samara region, Russia [5]Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Channing Laboratory, Boston, MA, USA [6]Pediatric Endocrine Division, Departments of Pediatrics and Cell Biology, University of Massachusetts Medical School, Worcester, MA, USA [7]Center for Demography and Human Ecology of Institute for Forecasting, Russian Academy of Sciences, Moscow, Russia [8]Center for Disease Control and Prevention, Atlanta, GA, USA [9]Ecological Analytical Center, Moscow, Russia

Introduction

Chapaevsk (population 72,000) is a small city located in central Russia (1200 kilometers south-east of Moscow) with an area of 187 km^2, half of which is occupied by chemical industries. The Khimprom Chemical Plant in Chapaevsk had produced chlorine-containing industrial and agricultural chemicals, which generated polychlorinated dibenzodioxins/dibenzofurans (PCDD/PCDFs) as industrial contaminants. Release of contaminants from this plant led to substantial PCDD/PCDFs (dioxin) pollution of the city's air, soil, water and food supply, including locally raised animals and vegetables, with continued human exposure from these contaminated sources[1]. A large proportion of the population lives in close proximity to the Khimprom Chemical plant complex. There is also environmental contamination with polychlorinated biphenyls (PCBs). The primary aim of the longitudinal Russian Children's Study is to examine the association of dioxins and PCBs with boys' physical growth and sexual maturation. We identified baseline predictors of serum dioxins and PCBs, and total toxic equivalents (TEQs) for PCDD/F/PCBs.

Materials and Methods

The Russian Children's Study is a prospective cohort study of 499 peri-pubertal boys, enrolled at ages 8 and 9 years from 2003 through 2005. The present analysis includes 477 boys with complete data on serum dioxins, furans and PCBs. The boys' initial study visit included physical examinations, blood sampling, and completion of health, dietary, lifestyle and mood questionnaires. The blood samples were kept at -20° Celsius until shipment on dry ice to the Centers for Disease Control and Prevention (CDC) for analysis. The chemical analyses were performed by the National Center for Environmental Health (NCEH), Centers for Disease Control and Prevention, Atlanta, GA by previously described methods[2,3,4]. TEQs were calculated for PCDD/PCDF/PCBs using both the WHO 1998 and 2005 toxic equivalency factors (TEFs). Those samples with measured values below the limit of detection (LOD) were imputed using the sample LOD/√2. General linear regression models, using a $\log_{10}$-transformation of the serum total concentrations of PCDD/PCDF/C-PCBs (co-planar PCBs), 2005 TEQs, and PCBs were used to assess associations with covariates, such as boy's age at examination, boy's body mass index (BMI; kg/m^2), duration of boy's breast feeding (weeks), mother's employment at Khimprom Chemical Plant, distance of current residence from center of Khimprom complex, maximal parental education, residence in Chapaevsk (years), mother's local gardening (ever vs. never), and consumption of local foods. Local food categories included eggs, dairy products, poultry, non-poultry meat, fish, and fruits and vegetables. Each food category was modeled as any local of foods within that category versus none, except for fruits and vegetables which was modeled as quintiles (in grams). Local food consumption was adjusted for total food consumption within that category, and each food category was modeled separately.

Results and Discussion:

Demographic Characteristics

At the baseline examination the boys were 8 (62%) or 9 (38%) years old, and the mean (SD) for BMI was 16.0 (2.4), duration of breast feeding was 27.6 (43.7) weeks, duration of residence in Chapvaesk was 5.4 (3.0) years, and distance of the current residence from the Khimprom plant was 4.2 (2.4) km. Of the study families 19% lived within 2 km of the center of the Khimprom plant complex, 38% reported household income of 7200 rubles/month or more, 32% of the parents were college graduates, 6% of mothers reported employment at the Khimprom plant, 60% reported local gardening. Local food consumption was led by fruit and vegetable consumption (92%), followed by dairy (46%), fish (21%), eggs (16%), poultry (7%), and non-poultry meat (5%).

Distribution of serum dioxins and PCBs

The distribution of the serum total PCDD/PCDF/C-PCBs was skewed to the right, with a median of 362 pg/g lipid (Table 1) and an extreme outlier of 2963 pg/g lipid (Figure 1). The congeners with the largest contributions were OCDD (23%), PCB 77 (21%), and PCB 126 (15%). The median of the serum total 2005 WHO TEQs was 21.1 pg/g lipid (Table 1), lower than the median (29.4 pg/g lipid) total 1998 WHO TEQs, primarily due to the reduction in toxic equivalency factors for M-PCBs (mono-ortho PCBs) (Figure 1). The congeners with the largest contributions to the serum total 2005 TEQs were PCB 126 (30%), dioxin 12378 (20%), and furan 23478 (17%). The median (25^{th}, 75 percentile) concentration for PCBs (excluding C-PCBs) was 249 (164, 393) ng/g lipids.

Predictors of serum dioxins and PCBs

Older age and longer duration of breast feeding were associated with significantly higher serum dioxins and PCBs, while higher BMI was associated with lower serum dioxins and PCBs. Boys whose mothers gardened locally, those whose mothers were employed at the Khimprom plant and boys who lived closer to the Khimprom plant had significantly higher serum dioxin and PCB concentrations. Higher maximum parental education was associated with significantly lower serum dioxin concentrations (Table 2) and marginally lower 2005 TEQs. Longer duration of residence in Chapaevsk was associated with higher serum 2005 TEQs and PCBs, but not with serum dioxin concentrations.

Dietary predictors of serum dioxins and PCBs

After adjustment for the above predictors, consumption of local eggs, poultry, non-poultry meat, and dairy were significantly associated with higher serum dioxins, PCBs, and total TEQs. Additionally, consumption of local fish was significantly associated with higher serum PCBs and total TEQs. There was a suggestion that boys consuming the highest level of local fruits and vegetables had higher serum total TEQs than those not consuming any local fruits or vegetables.

Conclusions:

Dioxins and PCBs are lipophilic, persistent environmental contaminants that bioaccumulate in the human body. Consistent with other studies, breast feeding was a predictor of these compounds in our analyses. Despite its narrow range, greater age was associated with higher serum levels of these compounds, as is seen in adult populations. We found that higher BMI was associated with lower serum levels of these compounds, but since our analysis is cross-sectional there is inherent uncertainty in interpreting this association. It may be that the lipophilic compounds are more likely to be sequestered in the body fat or that in growing children higher BMI signifies faster growth and dilution of dioxin-like compounds in a larger adipose reserve. Mother's employment at Khimprom, the putative source of environmental dioxins, was associated with higher serum concentrations of dioxins in the boys, and was also associated with higher serum concentrations of PCBs, compounds not known to be produced at Khimprom. Whether this represents a true source of PCB exposure, or is correlated with an unknown source, requires further investigation. Proximity of the current residence to Khimprom, even after adjustment for local food consumption and other covariates, was associated with higher serum levels of dioxins, furans, and PCBs. In particular, those

living within 2 km of Khimprom had average levels 29% higher than those more than 5 km from Khimprom. This could have important public health implications for the community, as many live close to the plant. Additionally, boys whose mothers garden locally have significantly higher serum levels of dioxins and PCBs, which may be through maternal transmission or exposure to contaminated soil.

The summary measures of dioxins and PCBs that we examined had most of the same predictors. However, maximum parental education was associated only with dioxin-like compounds. On the other hand, the summary measures (serum total PCBs, TEQs) that were composed of a high proportion or entirely of PCBs were positively associated with duration of residence in Chapaevsk and suggest that the local environment of Chapaevsk may be an important source of PCB exposure.

The consumption of local foods, especially eggs, was consistently associated with higher serum levels of dioxins, PCBs, and total TEQs. Further investigation should be undertaken to determine why specific food groups contribute to higher exposure. Additional analyses are planned to examine additional socioeconomic and environmental factors that may be associated with our currently identified predictors. Later analyses will make use of longitudinal information to clarify the association of predictors, such as BMI, with serum levels of dioxins and PCBs.

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Figure 1

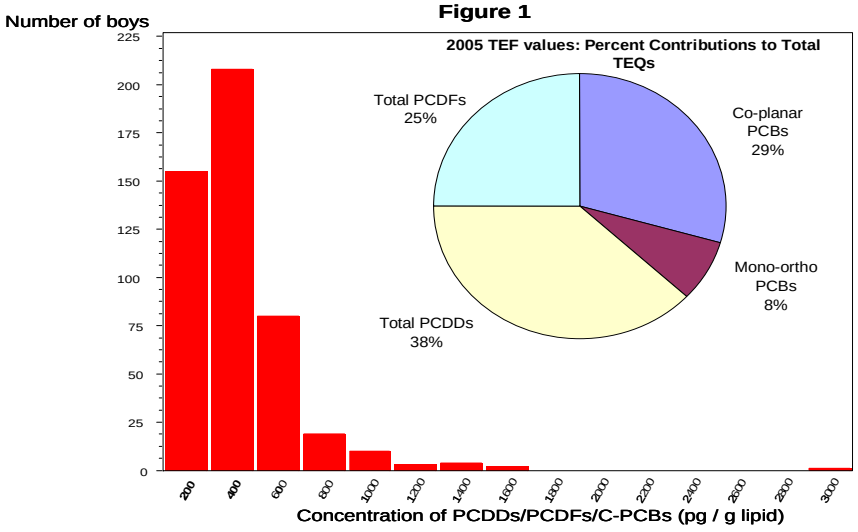

Table 1. Distribution of Serum Concentrations and 2005 WHO TEQs among 8-9 year old boys in the Russian Children's Study (N=482)

	Concentrations (pg/g lipid)					2005 WHO TEQs[1] (pg/g lipid)				
	Percentiles					Percentiles				
	Min	25th	Median	75th	Max	Min	25th	Median	75th	Max
2,3,7,8-TCDDs	0.3	1.3	2.8	3.9	44.9	0.3	1.3	2.8	3.9	44.9
Total PCDDs	23	93	136	189	1237	0.9	4.5	8.2	13.5	89.8
Total PCDFs	5	27	39	57	1083	0.4	3.0	4.2	6.9	154.3
Total C-PCBs	57	126	181	249	2067	0.5	4.5	6.4	9.4	67.2
Total M-PCBs	13	35	52	78	1560	0.4	1.1	1.6	2.4	46.8
Total PCDD/F/C-PCBs	123	278	362	499	2963	4.0	14.4	21.1	33.2	174.7

[1]TEQs include M-PCBs (2005 M-PCBs TEFs reduced to 0.00003)

Table 2. Multivariate Models predicting serum concentrations of log PCDD/PCDF/C-PCBs (pg/g lipid) among 8-9 year old boys in the Russian Children's Study (N=456)

Predictors	Estimate	S.E.	P-value	R^2 value
Age (years)	0.138	0.017	<0.0001	0.28
Body mass index (kg/m^2)	-0.019	0.004	<0.0001	
Duration of maternal breast feeding (weeks)	0.001	0.0002	<0.0001	
Mother's ever employed at Khimprom	0.082	0.036	0.02	
Maximum parental education level[1]	-0.038	0.014	0.006	
Mother's local gardening	0.038	0.017	0.02	
Distance from Khimprom (< 2 km)	0.112	0.023	<0.0001	
Distance from Khimprom (2 – 5 km)	0.029	0.018	0.12	
Distance from Khimprom (> 5 km)		Reference		
After adjustment for all of above, each individual food category:				
Any local egg consumption[2]	0.136	0.021	<0.0001	0.35
Any local meat consumption[2]	0.095	0.035	0.006	0.30
Any local poultry consumption[2]	0.073	0.031	0.02	0.30
Any local dairy consumption[2]	0.059	0.017	0.0004	0.32

[1]Ordinal: reference level=elementary/high school; junior/some college; college graduate+

[2]Separately included in multivariate model, adjusted for total consumption