Correlations among human plasma levels of polychlorinated biphenyls (PCBs) and dioxin-like compounds, and implications for epidemiologic studies

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Introduction

In a recent report from the Netherlands (1), among humans with background-only exposure to organochlorines, there were high correlations among tissue levels of dioxin-like compounds and those PCBs without dioxin-like activity. Whether this high correlation is present in other populations is unclear, but if it is present it has profound implications for measurement, confounding, and design in epidemiologic studies of the health effects of background ("normal") exposure to organochlorine compounds. In the present study, we examine the correlation among levels of various organochlorines in a sample of the Canadian population, and discuss the implications of the observed high correlations for epidemiologic studies.

Materials and Methods

In 1994 the Canadian Red Cross provided us with blood from 63 donors. The donors were from four cities: Hamilton (n=16), London (n=16), Montreal (n=16), and Quebec City (n=15). Thirty-three donors were female and 30 were male. The mean age was 45 with a range of 17 to 67 years.

The samples were analyzed for organochlorine compounds including mono- and di-ortho PCBs, non-ortho PCBs, polychlorinated dibenzodioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs). The analytical techniques (2) involved were solvent extraction, gravimetric lipid determination (3), defatting, purification with selected adsorbents, and identification and measurement with gas chromatography, with either mass spectrometric (MS) or electron capture detection. For brevity, the present analysis is focused on results for compounds and toxic equivalents (TEQs) summed within major chemical groups (mono- and di-ortho PCBs, non-ortho PCBs, PCDDs, and PCDFs).

Results and Discussion

The absolute levels of organochlorine compounds measured in these subjects (table 1) were similar to those previously reported for general populations in the U.S. and Canada (4).

The levels of mono- and di-ortho PCBs, non-ortho PCBs, PCDDs, PCDFs, and their corresponding total TEQs were fairly correlated (table 2)—in all cases the correlations among levels of these compounds were greater than 0.5.

These data suggest that in North America: 1) background levels of various organochlorine compounds are highly correlated at the present time, 2) one organochlorine measure may substitute for another, and 3) correct assessment of health effects of background exposure to a given compound may be difficult and may require that levels of related organochlorine compounds also be measured.

Data on the correlation of non-ortho PCBs, PCDDs, and PCDFs among themselves and with mono- and di-ortho PCBs are sparse, pertain to European populations, and are consistent with our findings (1,5). High correlations among levels of specific PCBs in U.S. (6,7) and European (1) populations have been reported previously.

The toxic effects of PCBs, PCDDs, and PCDFs occur by several mechanisms in laboratory animals. Dioxin and similarly-shaped (dioxin-like) compounds bind with the Ah receptor, and Ah receptor mediated toxicity accounts for most if not all dioxin effects (8). While some PCB congeners are dioxin-like, others are not. Non-dioxin-like PCBs are also toxic in animals, via mechanisms that are less clear. Nevertheless, both dioxin-like compounds and non-dioxin-like PCBs are sufficiently potent toxins in animal models that human health effects are plausible at background exposure levels, and human health effects of PCBs at background levels of exposure have been reported and are under investigation (9).

In technical epidemiologic terms, the implications of these findings are as follows. Suppose a given effect of background exposure to organochlorines is mediated entirely by a dioxin-like mechanism. In this instance failure to measure all of the key dioxin-like compounds in a study means the measured exposure is but a surrogate, and observed associations may be distorted. Because of the correlation among organochlorine levels, however, in some cases the distorted measure of effect may be considered acceptable and advantageous. For example, levels of total mono- and di-ortho PCBs may be used as a proxy, to estimate TEQ. This would require less sample and save resources. For several potential health outcomes, e.g. developmental neurotoxicity (10), PCB effects may occur both by mechanisms that are not Ah receptor mediated as well as by mechanisms that are. In such cases, associations observed between health effects and exposure to the major PCBs may be confounded by effects of non-PCB dioxin-like compounds. Because of the potential confounding, efforts to distinguish effects of specific organochorine compounds would benefit from large numbers of subjects to provide sufficient power.

While recent measures suggest that levels of mono- and di-ortho PCBs, non-ortho PCBs, PCDDs, and PCDFs are correlated in North Americans and Europeans, such correlations may not exist at other times or places. Populations with lower correlations may be of interest in attempts to sort out the contribution, if any, of various compounds to health effects. The high correlations in North America and Europe derive from the compounds being similarly concentrated within the food chain (11).

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Table 1. Median concentration in plasma of organochlorine compounds among 63 Canadian blood donors*

Compound	Median concentration (1^{st}, 3^{rd} quartiles)
Mono- and di-ortho PCBs (ng/g lipid)	
Total weight	262.9 (203.2 ,342.4)
Total weight in TEQs**	10.15 (7.61, 13.48)
Non-ortho PCBs (pg/g lipid)	
Total weight	98.6 (74.7 , 138.6)
Total weight in TEQs	3.31 (2.19, 6.04)
PCDDs (pg/g lipid)	
Total weight	776.9 (512.9 ,1035.5)
Total weight in TEQs	14.4 (10.8 , 17.9)
PCDFs (pg/g lipid)	
Total weight	35.9 (26.9 , 42.7)
Total weight in TEQs	5.89 (4.29, 7.40)
Total TEQs (pg/g lipid)***	34.9 (26.1 , 43.0)

* For levels below detection limit, a value of 0.5 times the detection limit was substituted. Abbreviations given in text.
** Units are pg/g lipid.
*** Based on sum of mono- and di-ortho PCBs, non-ortho PCBs, PCDDs, and PCDFs.

Table 2. Pearson correlation coefficients among log of concentrations of organochlorine compounds among 63 Canadian blood donors.*

	Total weights			Total weights in TEQs				
	N-O PCBs	PCDDs	PCDFs	M&DO PCBs	N-O PCBs	PCDDs	PCDFs	Total TEQs
Total weights								
M&DO PCBs	0.69	0.52	0.60	0.96	0.58	0.69	0.75	0.87
N-O PCBs		0.54	0.61	0.74	0.87	0.72	0.76	0.88
PCDDs			0.62	0.52	0.55	0.75	0.62	0.65
PCDFs				0.62	0.66	0.63	0.87	0.73
Total weights in TEQ								
M&DO PCBs					0.64	0.70	0.78	0.87
N-O PCBs						0.68	0.77	0.85
PCDDs							0.71	0.87
PCDFs								0.88

* Abbreviations and notes:
M&DO PCBs, mono- and di-ortho polychlorinated biphenyls;
N-O PCBs, non-ortho polychlorinated biphenyls;
other abbreviations are given in text.
Total TEQs is bsed on sum of mono- and di-ortho PCBs, non-ortho PCBs, PCDDs, and PCDFs.