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Polychlorinated Biphenyls in Prospectively Collected Serum and Parkinson's Disease Risk

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Abstract

Background—Evidence suggests possible Parkinson's disease (PD)-relevant neural effects of exposure to polychlorinated biphenyls. Limited epidemiological evidence suggests that polychlorinated biphenyl exposure may increase PD risk, but no studies have involved biomarkers of polychlorinated biphenyl exposure before PD onset. We examined the prospective association between serum polychlorinated biphenyls and PD.

Methods—We conducted a nested case-control study within the Finnish Mobile Clinic Health Examination Survey, with serum samples collected during 1968–1972, and analyzed in 2005–2007 for polychlorinated biphenyls. Incident PD cases were identified through the Social Insurance Institution's registry and confirmed by medical record review (n=101). Controls (n=349) were matched on age, sex, municipality, and vital status. We used logistic regression to estimate adjusted odds ratios.

Results—There was no evidence of increasing risk of PD with increasing polychlorinated biphenyl exposure in adjusted analyses. Instead, there was a trend toward lower odds of PD with increasing serum polychlorinated biphenyl concentrations, which was most pronounced for the sum of all measured polychlorinated biphenyl congeners and the sum of dioxin-like congeners. Compared with those in the lowest quintile, the odds ratio of PD among those in the highest

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quintile of total polychlorinated biphenyls was 0.29 (95% confidence interval: 0.12–0.70; p-trend=0.02) and for dioxin-like congeners was 0.34 (95% confidence interval: 0.13–0.90; p-trend=0.05).

Conclusions—These results do not support an increased risk of PD from polychlorinated biphenyl exposure, and instead suggest a possible protective effect of polychlorinated biphenyl exposure. Our findings may have implications for PD neuropathology, although alternative explanations should be considered.

Keywords

Epidemiology; prospective; Parkinson's disease; toxicology; organochlorines

INTRODUCTION

Several lines of evidence suggest a possible role for environmental risk factors for Parkinson's disease (PD).^{1, 2} Experimental evidence suggests that polychlorinated biphenyls (PCBs) can induce oxidative stress—a possible etiologic factor for PD,³ and impair dopaminergic transmission—a neuropathological hallmark of PD. Few studies have explored a possible role for PCBs in the development of PD. Increased risk of PD was found among a group of workers occupationally exposed to PCBs,⁴ and among heavier consumers of whale meat and blubber (a major route of exposure for PCBs) in the Faroe Islands.⁵ A small case-control study among Inuit in Greenland with high PCB exposure, however, found no association between plasma PCB concentration and PD.⁶ One study also found increased concentrations of PCB congener 153—and a similar trend for PCB 180 and total PCBs—in post-mortem caudate nucleus tissue from PD cases than controls,⁷ although a second study by the same group did not find differences from controls when looking at substantia nigra tissue.⁸ However, no prior studies of PCB exposure and PD have been prospective nor examined biomarkers of exposure collected many years before PD onset. We examined the association between serum PCB concentrations and PD in a case-control study nested within the Finnish Mobile Clinic Health Examination Survey (FMC), from which serum samples were collected from 1968–1972 and stored.

METHODS

Study population

The FMC was carried out in Finland during 1966–1972. Total populations in certain rural, semiurban, and industrial communities or random samples of them, comprising 62,440 adults aged 15 years or more, were invited to take part in the study (participation rate 82.5%).⁹ At baseline participants filled out a questionnaire and, for those recruited after June 15, 1968, blood samples were drawn (n=40,221), from which hematocrit and serum cholesterol determinations were performed. Serum samples were stored frozen at –20°C, which maintains the stability of serum PCBs.¹⁰ Cases and controls were selected from all participants without PD or psychosis who were 20–79 years of age at baseline. During follow-up to the end of 1994, 196 incident PD cases were identified. We randomly selected up to two controls per case (total n=349) among eligible participants who did not have PD and were alive at the time of the PD diagnosis of their matched case. The controls were individually matched for age, sex, vital status, and municipality, which also controls for the time of baseline examination and for the duration of serum sample storage because a given municipality was visited over a restricted time period.⁹ Most samples had been thawed once before thawing for the current study and so controls were also matched on number of prior sample thaws. For the current study serum samples were thawed and analyzed for PCBs in

2005–2007. The research was approved by the human subjects committee of the Harvard School of Public Health.

Case ascertainment

Cases (ICD-10 code G20) were identified through the Finnish nationwide registry of the Social Insurance Institution (SII) of patients receiving medication reimbursement, using the unique social security codes given to all citizens living in Finland. All people in Finland suffering from certain chronic disease, including PD, are eligible for free drug treatment. To get PD drug reimbursement, patients must provide a certificate written by the treating neurologist stating that all the diagnostic criteria for PD are met. This certificate must include symptom history and reports of clinical findings, including the presence of resting tremor, bradykinesia and/or muscle rigidity. An SII neurologist must agree with the diagnosis as described on the certificate for medication costs to be reimbursed. The medication allowance is not granted for patients with, for example, essential tremor, intention tremor or Parkinsonism caused by neuroleptics. Of 196 PD cases identified by this method, we were able to obtain the certificates for PD drug reimbursement and selected hospital records of 126 patients. These were re-evaluated retrospectively by our study neurologist (J.L.) according to the National Institute of Neurological Disorders and Stroke diagnostic PD criteria,¹¹ and blind to serum PCB concentrations. Neuropathologic data to confirm the diagnosis as definite was not available in any of the cases. Patients meeting the specified criteria for diagnostic confidence levels of both possible and probable PD were included. Cases either not meeting these criteria or with clinical features suggesting an alternative diagnosis were excluded. Of the 126 originally identified PD cases reviewed, 101 (80%) met criteria for PD, consistent with other estimates of the percentage of people clinically diagnosed with Parkinsonism in a general population that meet strict PD criteria.¹² The 25 originally identified PD cases excluded upon neurologist's review were excluded from all analysis. When the 70 cases we did not review were included in analyses, results were weaker.

Assessment of exposure

PCB analyses were performed by the Harvard School of Public Health Organic Chemistry Laboratory. Serum samples were sent and analyzed in groups of two or three—matched sets of a case and matched control(s)—and laboratory personnel were blind to case-control status. The analytic method used for PCB analysis used gas chromatography with dual electron capture detection, two capillary columns of different polarity and two internal standards as previously described.¹³ All samples were spiked with two surrogate compounds to monitor extraction efficiency and they were accompanied by procedural blanks, matrix spike samples, laboratory control samples and standard reference material (SRM). The laboratory has been successfully participating in international inter-comparison programs measuring PCB congeners in blood serum.

Samples were analyzed for 55 individual PCB congeners: International Union of Pure and Applied Chemistry (IUPAC) numbers 6, 8, 16, 18, 25, 26, 28, 31, 33, 37, 41, 44, 47, 49, 52, 60, 66, 70, 74, 84, 87, 95, 97, 99, 101, 105, 110, 118, 128, 135, 136, 138, 141, 146, 149, 151, 153, 156, 157, 167, 170, 171, 174, 177/201, 180, 183, 187, 189, 194, 195, 196, 199, 203, 206, 209. Final results were reported after subtracting the amount of the analyte measured in the procedural blank associated with the analytic batch. Mean procedural blank concentrations of the sum of all PCBs were below 0.02ng/g. The mean (sd) recoveries of the PCB#30 surrogate in all samples was 91% (5%) and for the PCB#204 surrogate was 85% (5%). The recoveries of all PCB congeners in matrix spike samples ranged from 84% to 98%. Laboratory control samples analyzed from the beginning to the end of sample analysis had concentrations of PCB congeners below 0.16ng/g, and the coefficients of variation for

55 PCB congeners were 17% with most congeners 10%. The results for PCBs in standard reference material (SRM1589a from National Institute of Standards and Technology, *Aroclor 1260 in Human Serum*) were all within 10% of the certified or assigned value ranges. Twenty samples were run blinded in triplicate and the coefficients of variation of the more common PCB congeners 118, 138, 153, and 180 ranged from 3.6%–4.6%. The coefficient of variation for the sum of all PCB congeners was 4.0%. Serum lipid content was determined from enzymatic measurements of total cholesterol and triglycerides using the Phillips formula.¹⁴

Statistical analyses

We estimated odds ratios (OR) of PD, and their 95% confidence intervals (CI) using conditional logistic regression. Since several originally identified cases were excluded because the diagnosis could not be confirmed, in order to include all controls we also used unconditional logistic regression with adjustment for matching factors (age, sex, and region) to estimate OR of PD, and 95% CI. Including all controls improves the precision of estimates and the adjustment for matching factors minimizes the bias towards the null that can arise when analyzing matched data with unconditional logistic regression.^{15, 16} We focused on the individual PCB congeners IUPAC 118, 138, 153, and 180 (the major congeners usually present and quantitated in PCB studies¹⁷); the sum of all measured PCB congeners; and a group that summed the concentrations of dioxin-like congeners (IUPAC 105, 118, 156, 157, 167, 189).¹⁸ We created quintiles of serum levels of PCBs as defined among the matched controls of the confirmed PD cases. Trends across quintiles were assessed by creating a continuous PCB concentration term by assigning to each participant the median value of their quintile of exposure, and PCB concentrations were assessed on a per gram serum basis with adjustment in the regression models for lipids (total serum cholesterol and serum triglycerides) because this approach has been found to minimize bias under the widest array of causal assumptions.¹⁹ Additional covariates included cigarette smoking (never, past, current, cigar/pipe only), body mass index (BMI: kg/m²), occupation (agriculture, industry, housewife, other), and serum dieldrin concentration.²⁰ All *p* values are two sided. Analyses were conducted with SAS software, version9 (SAS Institute, Inc., Cary, North Carolina). This study was approved by the Human Research Committee of the Harvard School of Public Health and the National Public Health Institute of Finland.

RESULTS

PCB 153 has been used to compare exposure levels across different studies because it is one of the most commonly measured congeners and because the sum of all PCB congeners is dependent on what congeners were measured in any given study. The median PCB 153 concentration among the controls matched to confirmed cases in FMC was 1.15ng/g serum, the 90th percentile was 2.28ng/g, and the geometric mean was 1.16ng/g. On a per lipid basis the median, 90th percentile, and geometric mean were 145, 283, and 148ng/g lipid, respectively. The distribution of other PCB congeners and groupings by case-control status is shown in Supplemental Table 1. Distributions of covariates among all cases, controls matched to confirmed cases, and all controls are shown in table 1. Slight variations in matching factors between confirmed cases and all controls are the result of some of the originally selected cases being deemed not PD upon further review and excluded while their controls were kept. The range of ages at baseline in our study sample was 26–79 years. Age and sex standardized distributions of covariates by quintiles of total PCBs among only the matched controls of the confirmed cases are shown in table 2. There was a notable increase in the percentage of males above the first quintile of total PCBs and decrease in the percentage of never smokers with increasing PCB exposure. The correlation among individual PCB congeners and PCB congener groupings was overall very high (Table 3).

In both unconditional and conditional logistic regression analyses there was a general trend towards lower odds of PD with increasing quintile of PCB exposure regardless of PCB congener or grouping (Table 4). This downward trend was most pronounced for the sum of dioxin-like congeners and total PCBs. Results of analyses adjusted only for age and sex, and analyses adjusted for all covariates except occupation are shown in Supplemental Table 2.

Results were similar when analyzing PCBs on a per lipid basis rather than by serum weight. Results for the sum of dioxin-like PCBs were also similar when summed based on their toxic equivalency factors.¹⁸ When analyses were restricted to never smokers, the results were similar. The OR of PD for those in the highest quintile of dioxin-like congeners, compared with the lowest among never smokers was 0.27 (95% CI: 0.07–1.04) using unconditional logistic regression, and for total PCBs was 0.30 (95% CI: 0.10–0.95). We also analyzed only those PD cases with onset more than the median (16.7) years after baseline in order to avoid possible reverse causation resulting from pre-clinical effects of the disease. The results were weaker for dioxin-like congeners, but similar for PCBs. The OR of PD for those in the highest quintile of dioxin-like congeners compared with the lowest was 0.73 (95% CI: 0.21–2.63) and for total PCBs was 0.23 (95% CI: 0.06–0.78), in unconditional logistic regression. Results were similar when stratified by sex, although slightly stronger among men. In unconditional logistic regression the OR of PD for those in the highest quintile of dioxin-like congeners compared with the lowest was 0.26 (95% CI: 0.07–0.98) among men and 0.38 (95% CI: 0.08–1.93) among women. The corresponding OR for total PCBs were 0.16 (95% CI: 0.04–0.66) among men and 0.36 (95% CI: 0.10–1.34) among women.

DISCUSSION

In this large nested case-control study with biomarkers of PCB exposure collected prospectively some two decades before disease, we found no evidence for increased odds of PD with increasing serum PCB concentration adjusting for age, sex, region, BMI, occupation, serum cholesterol and triglycerides, and serum dieldrin, the latter of which we have previously found to be associated with higher odds of PD in this population.²⁰ In contrast, there was evidence for a decreased risk of PD with increasing serum PCB concentrations. There was a high level of correlation among PCB congeners and congener groupings, and the results appeared most pronounced and consistent for the sum of dioxin-like congeners and the sum of all PCB congeners.

The exposure levels of the FMC cohort were much higher than is found in more recent general US populations. The median US concentration of PCB 153 found in data from those at least 20 years old in 2001–2002 in the National Health And Nutrition Examination Survey (NHANES) is 0.22ng/g serum and the 90th percentile is 0.67ng/g serum.²¹ The median concentration of PCB 153 in our FMC controls was also higher than most all other study settings where concentrations in general population samples have been determined.¹⁷ Only samples from a study population in the Faroe Islands from 1994–1995 were higher, a result of the high level of consumption of whale blubber in which PCBs bioaccumulate. PCB 153 serum concentrations in the FMC population were much closer to concentrations that have been found in occupationally exposed workers some 30 years after their occupational exposures.²²

Experimental animal studies have found that PCB exposure can reduce dopamine levels or dopamine transporter levels in several species,^{23, 24} which has led to speculation that PCB exposure may be a risk factor for PD. There is also evidence from human brain imaging studies that among PCB exposed workers there is a relation between higher serum PCB concentration and lower dopamine transporter density in the basal ganglia, although this

association was restricted to women.²⁵ A couple of post-mortem studies have looked at PCB concentrations in PD and control brains, with one finding higher concentrations than controls,⁷ but the other only seeing higher concentrations relative to patients with cortical Lewy body dementia.⁸ Inferring prior causality from such studies, however, is difficult. The epidemiological literature on such an association is limited, with results also suggestive, but equivocal.^{4–6} One study used standardized mortality ratios (SMR) to compare former capacitor factory workers—an occupation with high PCB exposure, which was demonstrated in a subset of the workers—with the general US population.⁴ Overall, there was not an elevated SMR for PD in these workers, although women deemed highly exposed via a job-exposure matrix did have a significantly elevated SMR for PD. The case assessment in this study, however, was from death certificate data, which is not ideal for a disease that can have a long duration like PD. A second study in the Faroe Islands found an increased OR of PD with higher adulthood consumption of whale meat and blubber, which are routes of exposures to many persistent pollutants including PCBs.⁵ However, in this setting with this exposure assessment, the exposure cannot be isolated to PCBs. Serum PCB concentration was not associated with PD, but the samples were necessarily collected after the development of PD. Similar null findings for plasma PCB concentrations were also found in a small case-control study among the Inuit of Greenland who have high PCB exposures from their diet.⁶

An inverse association between an exogenous exposure and risk of PD is not without precedent—for example, such an inverse association is well established for cigarette smoking.²⁶ In our study population there was a reasonably strong age and sex adjusted association between total serum PCB and cigarette smoking, which raises concern that our results for PCBs could be confounded by smoking particularly since we did not have detailed data on duration or intensity of smoking. If either of these were associated with more PCB exposure, this could introduce residual confounding. Such confounding is argued against somewhat by the fact that the results were similar among never smokers. Most smokers take up smoking at early ages, thus there would likely be few never smokers at baseline who later started smoking. While we cannot rule out confounding by other unmeasured variables, there are certain mechanisms of PCB action that perhaps deserve consideration for further inquiry as possibly providing some neuroprotective action in the context of PD.

The toxicity of PCBs has focused on their action at the aryl hydrocarbon receptor (AhR). These actions are mostly mediated by the coplanar or dioxin-like congeners that are in fact thought to have more limited neurotoxicity.²⁷ However, PCBs are metabolized by, and inducers of, CYP enzymes, in particular through activation of the AhR.²⁸ This is of interest given that cigarette smoking is an inducer of CYP enzymes—including 1A, which is also highly inducible by dioxin-like PCBs^{28, 29}—and it has been proposed that this may play a role in the protective association seen for cigarette smoking and PD.³⁰ In contrast to the coplanar PCBs, the ortho-substituted or non-coplanar PCB congeners have several mechanisms of action that could be neuroactive, with the possibility of neuroprotection.^{27, 31} First, some PCB congeners have estrogenic effects, and some of their hydroxyl-PCB metabolites not only also have estrogenic effects themselves, but also inhibit enzymes that metabolize estrogen.^{32, 33} Estrogen has been suggested to be neuroprotective in the context of PD,^{34, 35} thus providing a possible protective mechanism for PCBs. Second, some PCBs and hydroxy-PCB metabolites can lead to mitochondrial uncoupling.^{36, 37} While this uncoupling reduces production of ATP and so can be toxic, some uncoupling can be counteracted—and ATP levels restored—by a compensatory upregulation of PGC-1alpha.³⁸ Overexpression of PGC-1alpha has recently been shown to block dopaminergic neuron loss normally induced by the alpha-synuclein mutation or exposure to the pesticide rotenone.³⁹

A major strength of our study includes the assessment of PCB exposure many years prior to PD before biological or behavioral changes related to the disease itself are likely to affect serum PCB concentrations. However, while PCBs are persistent and therefore serum levels are a reasonable biomarker for past cumulative exposure, it is a limitation that variations in exposure to PCBs after FMC blood collection are not captured. Such variations could introduce measurement error to the extent that past exposures do not predict future exposures. This possible misclassification is minimized somewhat because use of PCBs in Finland stopped in the 1970's, shortly after FMC blood samples were collected, but although measures of PCBs in the environment declined after this, the persistence of PCBs in the environment still means exposures could have continued.⁴⁰ We also did not have follow-up data on confounders. Our PD case definition could not involve physical examination. Instead, we relied on reports from the treating neurologist submitted for the patient to obtain reimbursement for PD medications and then our study neurologist re-reviewed these files to further confirm the cases. Although some diagnostic misclassification may have occurred, error from this source is probably modest; clinico-pathological studies show about 90% accuracy of clinical PD diagnosis made by neurologists.⁴¹ Furthermore, diagnostic errors are probably unrelated to serum PCB concentration, and would thus tend to attenuate any true association. Lastly, although the results are restricted to the Finnish population, we have no reason to expect that the results would not apply to other similarly exposed populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline characteristics by case control status.

	Confirmed Cases (n=101)	Matched Controls* (n=186)	All Controls† (n=349)
Age, mean (sd)	49.7 (9.9)	49.4 (9.8)	52.8 (10.4)
Years to PD diagnosis, mean (sd)	16 (6)	--	--
BMI, mean (sd)	26.7 (3.8)	25.8 (3.7)	26.0 (3.8)
SBP, mean (sd)	144 (19)	144 (24)	147 (25)
DBP, mean (sd)	84 (11)	82 (11)	83 (12)
Serum cholesterol, mean (sd)	264 (51)	273 (54)	271 (52)
Serum triglycerides, mean (sd)	124 (50)	135 (80)	135 (71)
Male, n (%)	47 (46.5)	92 (49.5)	192 (55.0)
Cigarette smoking, n (%)			
Never	68 (67.3)	102 (54.8)	183 (52.4)
Past	17 (16.8)	29 (15.6)	59 (16.9)
Current	16 (15.8)	49 (26.3)	96 (27.5)
Cigar/Pipe only	0 (0)	6 (3.2)	11 (3.2)
Hypertension, n (%)			
Normal	39 (38.6)	80 (43.0)	137 (39.3)
Borderline	47 (46.5)	88 (47.3)	163 (46.7)
Mild	6 (5.9)	6 (3.2)	12 (3.4)
Definite	9 (8.9)	12 (6.5)	37 (10.6)
Region, n (%)			
Southwest	10 (9.9)	20 (10.8)	43 (12.3)
Southern	14 (13.9)	28 (15.1)	71 (20.3)
Central	13 (12.9)	20 (10.8)	30 (8.6)
Western	8 (7.9)	16 (8.6)	32 (9.2)
Eastern	35 (34.7)	63 (33.9)	106 (30.4)
Northern	21 (20.8)	39 (21.0)	67 (19.2)

* For the 101 confirmed cases.

† For all 196 potential PD cases.

Table 2

Baseline characteristics* by quintile of total serum PCB concentration (ng/g serum) among controls matched to confirmed PD cases.

	Q1	Q2	Q3	Q4	Q5
Total PCB, mean (ng/g)	3.33	4.77	6.16	7.87	13.93
Age, mean (sd)	47.8 (9.3)	51.0 (8.3)	51.1 (11.6)	48.8 (9.9)	48.4 (9.3)
Male, %	5 (16.1)	17 (47.2)	20 (51.3)	23 (63.9)	27 (61.4)
BMI, mean (sd)	26.7 (4.3)	26.0 (3.3)	26.4 (3.1)	26.2 (4.0)	25.1 (3.6)
SBP, mean (sd)	141 (15)	141 (19)	148 (21)	149 (26)	144 (24)
DBP, mean (sd)	85 (10)	83 (11)	82 (11)	84 (10)	81 (12)
Serum cholesterol, mean (sd)	235 (48)	258 (55)	288 (54)	277 (49)	288 (53)
Serum triglycerides, mean (sd)	111 (39)	118 (36)	148 (58)	137 (69)	156 (110)
Never cigarette smoker, %	78.0	67.5	57.1	44.4	46.9
Nonotensive, %	37.7	43.5	33.5	38.7	46.1
Occupation					
Agriculture	37.9	28.7	8.1	13.6	27.5
Industry	19.1	29.7	44.7	41.6	35.3
Housewife	3.8	12.2	14.8	1.9	2.2
Other	39.2	29.4	26.3	39.1	35.0
Region, %					
Southwest	10.4	12.5	9.0	12.4	4.6
Southern	7.8	14.2	28.5	9.4	14.7
Central	20.6	20.5	12.7	3.9	7.5
Western	12.7	7.2	9.6	7.7	9.7
Eastern	41.1	37.0	31.0	25.2	28.2
Northern	7.4	8.6	9.3	41.4	35.2

* All variables, except age and sex, are age and sex adjusted by direct standardization to all matched controls.

Table 3

Spearman correlations between PCBs (ng/g lipids) among controls matched to confirmed cases in the Finnish Mobile Clinic, 1968–1972.

	PCB 138	PCB 153	PCB 180	Total PCBs	Dioxin-like
PCB 118	.84	.84	.74	.65	.97
PCB 138		.99	.93	.79	.92
PCB 153			.96	.80	.92
PCB 180				.78	.85
Total PCBs					.71

All correlations $p < 0.0001$.

Table 4

Multivariable adjusted* odds ratio (OR) (95% confidence interval) for Parkinson's Disease by quintile (Q) of PCB concentration (ng/g serum).

Congener	Q1	Q2	Q3	Q4	Q5	p-trend
PCB 118, range[†] (ng/g serum)	<0.234	0.234–0.287	0.288–0.360	0.361–0.460	0.460–1.387	
Unconditional model [#]	Ref	0.54 (0.26–1.12)	0.64 (0.30–1.36)	0.68 (0.31–1.46)	0.37 (0.14–0.95)	0.10
Conditional model ^{\$}	Ref	0.73 (0.32–1.63)	0.76 (0.33–1.75)	0.65 (0.28–1.52)	0.38 (0.12–1.25)	0.13
PCB 138, range[†] (ng/g serum)	<0.438	0.489–0.631	0.632–0.820	0.829–1.157	1.157–3.630	
Unconditional model [#]	Ref	0.80 (0.38–1.66)	0.66 (0.30–1.45)	0.56 (0.23–1.35)	0.43 (0.16–1.14)	0.09
Conditional model ^{\$}	Ref	0.86 (0.36–2.04)	0.64 (0.26–1.61)	0.61 (0.22–1.67)	0.41 (0.12–1.42)	0.16
PCB 153, range[†] (ng/g serum)	<0.768	0.769–1.016	1.020–1.346	1.347–1.882	1.884–5.211	
Unconditional model [#]	Ref	0.79 (0.38–1.65)	0.67 (0.31–1.49)	0.66 (0.28–1.56)	0.36 (0.13–1.00)	0.06
Conditional model ^{\$}	Ref	0.72 (0.29–1.78)	0.66 (0.26–1.64)	0.65 (0.23–1.87)	0.28 (0.07–1.07)	0.08
PCB 180, range[†] (ng/g serum)	<0.436	0.436–0.620	0.620–0.813	0.813–1.133	1.137–3.071	
Unconditional model [#]	Ref	1.05 (0.50–2.23)	0.81 (0.34–1.89)	0.46 (0.18–1.22)	0.53 (0.19–1.53)	0.12
Conditional model ^{\$}	Ref	1.53 (0.60–3.91)	1.24 (0.44–3.53)	0.58 (0.19–1.78)	0.65 (0.17–2.43)	0.17
Sum of Dioxin-like congeners, range[†] (ng/g serum)	<0.404	0.405–0.516	0.516–0.641	0.645–0.829	0.831–2.228	
Unconditional model [#]	Ref	0.68 (0.34–1.38)	0.63 (0.30–1.33)	0.65 (0.29–1.45)	0.34 (0.13–0.90)	0.05
Conditional model ^{\$}	Ref	0.85 (0.39–1.83)	0.60 (0.27–1.36)	0.62 (0.25–1.52)	0.32 (0.10–1.05)	0.04
Total PCBs, range[†] (ng/g serum)	<4.56	4.56–5.79	5.81–7.46	7.49–10.00	10.01–82.10	
Unconditional model [#]	Ref	0.45 (0.22–0.94)	0.50 (0.23–1.08)	0.54 (0.24–1.21)	0.29 (0.12–0.70)	0.02
Conditional model ^{\$}	Ref	0.43 (0.17–1.08)	0.53 (0.21–1.29)	0.53 (0.19–1.46)	0.28 (0.09–0.90)	0.08

* Adjusting for matching factors age, sex, and region (by stratification in the conditional logistic model), as well as smoking, BMI, triglycerides, cholesterol, occupation, and serum dieldrin concentration.

[†] Among 101 cases and 349 controls.

[#] 101 cases, 349 controls.

^{\$} 101 cases, 186 controls.