# Comparison of Polychlorinated Biphenyl Levels across Studies of Human Neurodevelopment

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**Polychlorinated biphenyls (PCBs) are persistent pollutants that are ubiquitous in the food chain, and detectable amounts are in the blood of almost every person in most populations that have been examined. Extensive evidence from animal studies shows that PCBs are neurotoxins, even at low doses. Interpretation of human data regarding low-level, early-life PCB exposure and subsequent neurodevelopment is problematic because levels of exposure were not similarly quantified across studies. We expressed the exposure levels from 10 studies of PCB and neurodevelopment in a uniform manner using a combination of data from original investigators, laboratory reanalyses, calculations based on published data, and expert opinion. The mainstay of our comparison was the median level of PCB 153 in maternal pregnancy serum. The median concentration of PCB 153 in the 10 studies ranged from 30 to 450 ng/g serum lipid, and the median of the 10 medians was 110 ng/g. We found that *a*) the distribution of PCB 153 exposure in most studies overlapped substantially, *b*) exposure levels in the Faroe Islands study were about 3–4-fold higher than in most other studies, and *c*) the exposure levels in the two recent U.S. studies were about one-third of those in the four earlier U.S. studies or recent Dutch, German, and northern Québec studies. Our results will facilitate a direct comparison of the findings on PCBs and neurodevelopment when they are published for all 10 studies. *Key words:* child development, environmental exposure, environmental pollutants, neurotoxins, polychlorinated biphenyls. *Environ Health Perspect* 111:65–70 (2003). [Online 2 December 2002]**

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Polychlorinated biphenyls (PCBs) are persistent pollutants that are ubiquitous in the food chain, and detectable amounts are in the blood of almost every person in most populations that have been examined. Extensive evidence from animal studies (*1*) shows that PCBs are neurotoxins, even at low doses (*2*), and several plausible biologic mechanisms of action have been identified (*3,4*). Human exposure *in utero* to high levels of heat-degraded PCBs is almost certainly neurotoxic (*5*).

Whether prenatal and infant exposure to background levels of PCBs is detrimental for human neurodevelopment has been under investigation for nearly 20 years (*6*). Statistically significant associations were found between PCB exposure and child neurodevelopment and cognition in some studies (*7–11*) but not others (*12–14*). The variation in results across studies could be caused by any number of factors. For example, *a*) favorable aspects of the early child-care setting could protect some groups against ill effects of PCBs; *b*) a high rate of exposure for a limited time could be more toxic than chronic low-level exposure even though both result in equivalent PCB levels; *c*) differences existed in the neurodevelopmental testing protocols; *d*) the composition of the PCB mixture in subjects could have varied across studies; or *e*) the association with PCBs was confounded or modified by concurrent exposures (e.g., methylmercury, omega-3 fatty acids) in a manner that varied across studies and these exposures were not assessed consistently across studies. But foremost among the possible explanations for the variation in findings across studies is that the degree of PCB exposure differed. This possibility, however, has been difficult to assess because methods of measuring and reporting PCB exposure have differed. Interpretation of data on PCBs and neurodevelopment would be more straightforward if levels of exposure were similarly or identically quantified. The present report is devoted entirely to an analysis of the relative levels of exposure in all studies of background-level PCB exposure and neurodevelopment.

The variation in reported PCB levels across studies stems partly from real differences in exposure levels across populations and calendar time, but there were also differences in type of specimen analyzed, sample extraction, chromatography, method of quantification, and data handling and presentation (*6*).

Sometimes the contribution of measurement techniques to the variation in PCB exposures reported across studies can be assessed by either sending each laboratory an aliquot from one large pool or by having material from each study analyzed at one central laboratory. Neither of these strategies, however, was an option for evaluating relative exposure across the entire group of studies on PCBs and neurodevelopment. Some of the laboratories or methods used to analyze the specimens are no longer operational. Furthermore, biologic specimens were no longer available from all studies. Because a direct laboratory-based comparison of exposure levels across all studies

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was not possible, we expressed the PCB levels from studies of neurodevelopment in a uniform manner using a combination of data from original investigators, laboratory reanalyses, calculations based on published data, and expert opinion. We then compared the PCB levels across studies and assessed the extent to which true or technical differences accounted for the variation. Despite the potential drawbacks of our approach, it had the advantage of feasibility, and, we believe, it provided a reasonable indication of the relative exposure levels in the various studies considered.

## Methods

Investigators from each study of PCBs and neurodevelopment of which we were aware (Table 1) contributed to this study and agreed on a protocol for parallel presentation of data. The subjects were from North America, the European continent, and the Faroe Islands, located in the Atlantic Ocean northeast of Scotland. The samples had been collected over a span of about 40 years. The northern Québec and Faroe Island populations are from cultures that consume large amounts of marine foods. The Michigan and New York subjects included more freshwater fish eaters than the general U.S. population has.

The type of specimen originally selected for analysis varied across laboratories such that no single specimen type was analyzed in all studies (Table 1). We therefore chose to use data for maternal serum (or plasma) where possible and, when not possible, to use data for maternal milk levels. For those studies where we used data for maternal milk, we reexpressed the levels as maternal serum levels, using a conversion factor described below. We chose to express all levels as if they were in serum so that they could be easily compared with those in populations for whom measures in breast milk were not feasible (e.g., men).

For the specimen type specified for each study (Table 1), we began with the 5th, 25th, 50th, 75th, and 95th percentiles of the distributions of PCB 153 concentration, and the ratio of median PCB 118 and median PCB 153 concentrations. PCBs 118 and 153 are designated by their IUPAC (International Union of Pure and Applied Chemistry) numbers (*19*).

The mainstay of our comparison was the median level of PCB 153 across studies. We adopted this approach because *a*) comparison of the level of a specific congener instead of the level of the sum of quantitated PCBs was free from comparability issues caused by quantitation of differing numbers of congeners (Table 2); *b*) quantitation of PCB 153 levels is relatively straightforward because it is always among the PCB congeners present at the highest concentration; *c*) coelution by other congeners, if any, is relatively minor; and *d*) PCB 153 constitutes a large portion of the sum of quantitated PCBs in all studies. The correlations between the concentration of PCB 153 and the sum of quantitated PCBs reported have been high: 0.96 (*20*), 0.89 (*21*), and 0.97 (*22*).

We compiled information about laboratory methods and method of data handling, supplementing published material, so that detailed information was available for each study (Table 2). The number of specific congeners quantitated varied, with the maximum being 68. Most of the studies providing PCB measures in milk used a gravimetric procedure to assay lipids.

***Methods used in reexpression of results.*** As noted above, the data on PCB levels available to us were not all directly comparable. Thus, in several cases, we had to reexpress the data. The methods used to estimate conversion factors are described here.

Two studies on PCBs and neurodevelopment (*7,8*) were done when packed column gas chromatography analyses were standard.

**Table 1.** Characteristics of the studies on PCBs and neurodevelopment.

| Reference number | Location of population | Years specimens collected | Type of specimen[a] | | | Specimen used in the present study | Number of specimens[b] |
|---|---|---|---|---|---|---|---|
| | | | Maternal serum, plasma | Maternal milk | Cord serum | | |
| (*15*)[c] | U.S./11 cities | 1959–1965 | + | – | – | Maternal serum | 2,737 |
| (*16*)[c] | U.S./California | 1964–1967 | + | – | – | Maternal serum | 399 |
| (*7*) | U.S./North Carolina | 1978–1982 | + | + | + | Maternal serum | 872 |
| (*8*) | U.S./Michigan | 1980–1981 | + | + | + | Maternal serum | 196 |
| (*9*) | Netherlands/2 cities | 1990–1992 | + | + | + | Maternal plasma | 415 |
| (*10*) | U.S./New York | 1991–1994 | – | + | + | Milk | 50 |
| (*11*) | Germany/Düsseldorf | 1993–1995 | – | + | + | Milk | 126 |
| (*17*)[c] | U.S./Massachusetts | 1993–1998 | – | + | + | Milk | 160 |
| (*12*) | Denmark/Faroe Islands | 1994–1995 | + | + | + | Maternal serum | 173 |
| (*18*)[c] | Canada/Northern Québec | 1995–1998 | + | + | + | Maternal plasma | 159 |

[a]Type of specimen in which PCB levels were measured. [b]Number of specimens on which reported or estimated PCB levels were based, which is not necessarily the same as the number of children studied. [c]References for these studies are for initial publications; results for neurodevelopmental outcomes are not yet published.

**Table 2.** Characteristics of the laboratory and data handling methods among studies of PCBs and neurodevelopment.

| Reference number | Reference location | Method | | | Number of congeners qualitated | Recovery | | Method of lipid analysis | Median PCB 118/median PCB 153[b] |
|---|---|---|---|---|---|---|---|---|---|
| | | Extraction (phase) | Cleanup | Gas chromatograph separation | | Percent | Adjusted[a] | | |
| (*15*)[c] | U.S./11 cities | Solid | Florisil | High resolution | 11 | ~65 | No | Enzymatic | 0.87 |
| (*16*)[c] | U.S./California | Liquid | Florisil | High resolution | 11 | 66 | Yes | Enzymatic | 0.58 |
| (*7*) | U.S./North Carolina | Liquid | Florisil | Packed column | NA[d] | > 90 | Yes | ND[e] | 0.51 |
| (*8*) | U.S./Michigan | Liquid | Florisil | Packed column | NA | NK | No | ND | 0.32 |
| (*9*) | Netherlands/2 cities | Liquid | Florisil | High resolution | 4 | > 95 | No[f] | ND | 0.18 |
| (*10*) | U.S./New York | Liquid | Florisil | High resolution | 68 | 77 | Yes | Gravimetric | 0.23 |
| (*11*) | Germany/Düsseldorf | Solid–liquid | Florisil | High resolution | 3 | 85 | No | Photometric | 0.20 |
| (*17*)[c] | U.S./Massachusetts | Liquid | Silica gel[g] | High resolution | 50 | 95 | No | Gravimetric | 0.47 |
| (*12*) | Denmark/Faroe Islands | Solid | Florisil | High resolution | 28[h] | ~65 | No | Enzymatic | 0.27 |
| (*18*)[c] | Canada/Northern Québec | Liquid | Florisil | High resolution | 14 | > 95 | No | Enzymatic | 0.14 |

Abbreviations: NA, not applicable; ND, not determined; NK, not known.
[a]Adjusted refers to whether or not the reported PCB levels had been adjusted for recovery. [b]Ratio of median concentrations; for reference (*8*) this is a ratio of means; for reference (*18*) this is a ratio of geometric means. [c]References for these studies are for initial publications; results for neurodevelopmental outcomes are not yet published. [d]Not applicable for packed column method. [e]Serum lipids not determined. [f]Whether recovery adjustment was done was not specified in published reports and no further information was available; no adjustment assumed. [g]Aluminum oxide was also used in the cleanup. [h]In reference (*11*), the original authors calculated the sum of PCBs as 2 × (sum of PCBs 138, 153, and 180).

The relation between PCB measures obtained using packed column methods and those from modern high-resolution (congener-specific) capillary column gas chromatographic methods was estimated using results from two small studies where samples were analyzed both ways.

The PCBs in the samples from the North Carolina study (*7*) were originally quantitated using a "two-peak" packed column method (*23*). Aliquots of the original specimens have been frozen at –20°C since collection. In 1998, aliquots of milk specimens collected several days after delivery were selected for 10 subjects. The 10 were chosen to span the range of PCB levels originally measured. These specimens were analyzed at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, using high-resolution capillary column gas chromatography–mass spectroscopy. Results were obtained for 36 specific PCB congeners (*24*). For the 10 specimens analyzed by both methods, the ratio of the sum of 36 congeners quantitated by the CDC to the value obtained by the original "two-peak" method had a median of 0.38 (range, 0.20–0.82); the Pearson correlation coefficient for the sum of quantitated PCB levels measured by the two methods was 0.95. Based on the CDC results, the ratio of the concentration of PCB 153 to the sum of 36 congeners for the 10 specimens had a median of 0.17 (range, 0.14–0.21). Therefore, to reexpress the "two-peak" results for the North Carolina study in terms of the values that would have been obtained by high-resolution methods, we multiplied the original values by 0.38. Similarly, estimates of the amounts of PCB 153 were obtained by further multiplying the estimated sum of PCB values by 0.17.

PCBs in the samples from the Michigan study (*8,25*) were originally quantitated using a packed column method based on eight chromatographic peaks. The same method was used a few years later on blood samples obtained from the same children at 4 years of age, and a subset of blood from the 4-year-olds was also analyzed by a high-resolution method (*26*). Two serum pools were created: one composed of aliquots of equal volume from 11 female 4-year-olds, and a second composed of the same for nine male 4-year-olds. Both pools were analyzed by the same high-resolution method and the levels of more than 14 specific congeners were quantified. The results were compared with the mean PCB level quantitated by the packed column method among the subjects in each pool. For the two pooled specimens, the ratio of the sum of PCBs obtained by the high-resolution method to the value obtained by the packed column method had a median of 1.1. In addition, the congener-specific results showed that the ratio of the concentration of PCB 153 to the sum of PCBs for the two specimens had a median of 0.18. Therefore, to reexpress the original packed column results for the Michigan study in terms of the values that would have been obtained by high-resolution methods, we took the original values and multiplied them by 1.1, and further multiplied them by 0.18 to estimate levels of PCB 153.

Because PCBs are lipophilic, their levels are often expressed per gram of lipid in the tissue examined. We reexpressed the wet-weight PCB levels (μg/L serum) reported in three studies (*7–9*) as levels per gram of serum lipid. For the first two studies, we assumed that the third-trimester serum lipid levels were 7.9 g/L, the median of the median serum lipid levels among the five studies in which serum lipids were measured (*27*). For the third study, the serum cholesterol and triglyceride values were measured among half the subjects (data not shown). We assumed that the median serum lipid level in the Dutch subjects with lipid measures (8.4 g/L), estimated using Phillips et al.'s equation (*27*), was the same as for those without a lipid measure. We used the estimated median lipid level among those with a measure to reexpress the wet-weight PCB levels for all the Dutch subjects as levels per gram of serum lipid.

Three studies had milk but not serum PCB measures available. To reexpress milk PCB levels (ng/g lipid) as maternal serum PCB levels (ng/g lipid), we first identified other studies with "simultaneous" measures of both. Most had been published (*24,28,29*), but for two studies (Québec, Faroes) unpublished data were used. Based on the 14% drop in median milk PCB levels (fat basis) from birth to 6 weeks later, observed by Rogan et al. (*28*), we assumed that milk PCB levels decreased by 5% in the first 2 weeks after birth, and therefore multiplied the Dutch milk values (collected 2 weeks after birth) by 1.05 so that they would represent the levels at birth, as in the other studies. The ratio of the median PCB concentration (lipid basis) in milk to serum in the five studies (0.79, 1.31, 1.34, 1.59, 1.77) had an unweighted median value of 1.34. Published correlations between milk and serum PCB levels were 0.64 (*28*), and depending on the congener considered, 0.70–0.79 (*29*) and 0.62–0.99 (median, 0.90) (*18*).

The percentage of PCB recovered by the analytical procedures varied across studies (Table 2). Most studies either had high recovery or results adjusted for recovery. The two studies that used solid-phase extraction exclusively (*12,15*) had lower recoveries, and the reported PCB values were not recovery adjusted. To make these values more comparable with levels from other studies, we multiplied the reported values by 1/0.60 for PCB 153 and 1/0.67 for PCB 118 (*30*).

***Additional information on the effect of PCB quantitation methods.*** Our reexpression of packed column results as high-resolution results was based on data from a limited number of specimens analyzed by both methods. To assess the reasonableness of the conversion factors used, we also considered additional data that bear on this issue.

First, we estimated the relation between the PCB levels as quantitated by the original packed column methods (*7,8*). Thus, for 24 specimens from the North Carolina study (*7*) that had been quantitated using the "two-peak" method (*22*), the original laboratory results (chromatograms and corresponding computer printouts) were reviewed by an analytical chemist (M.S.W.), and the results were quantitatively reexpressed using the "eight-peak" method used in the Michigan study (*8*). Ordinary least squares regression showed that PCB levels obtained using the "two-peak" method gave results that were 2-fold higher than those obtained using the "eight-peak" method (Pearson $r = 0.98$). This factor-of-two difference between the two approaches has been confirmed independently by Jensen (*31*). Because the factor to convert the "two-peak" results to high-resolution results was 0.38, and for the "eight-peak" results was 1.1, the ratio we obtained based on our small number of analyses was 1.1/0.38, or 2.9. With the expected value being 2, we have some indication of the potential degree of error in our conversions.

The ratio of PCB concentrations measured by high-resolution compared with packed column methods has been examined by various investigators, who have reported values ranging from 0.5 to 1.0, with most ratios being less than 1.0 (*32*). These ratios are based on typical packed column methods, which use about eight peaks in quantitation. Thus, the ratio of 1.1 for the Michigan data is consistent with at least some reported values, even if slightly higher. If the North Carolina study had used an eight-peak method of quantitation, the conversion factor for their study (high resolution to packed column) would be 0.38 × 2, or 0.76, which is also consistent with the reported values.

## Results

The median concentration of PCB 153 in the 10 studies ranged from 30 to 450 ng/g serum lipid (Table 3; Figure 1), and the unweighted median level across the 10 studies ("overall median") was 110 ng/g. The median PCB 153 level in the Faroe Islands was 4-fold greater than the overall median. The median PCB 153 levels in Massachusetts and New York, the most recent U.S. studies, were about one-quarter and one-third of the overall

median, respectively. Median levels of PCB 153 in the Dutch, German, and Québec studies were similar to those in the earlier U.S. studies. Within individual studies, the ratio of the 95th to the 5th percentiles of PCB 153 concentration ranged from 3.8 (California) to 12.3 (Québec), with a median of 7.5.

One set of assumptions that we made in our calculations pertained to the factors used to reexpress packed column results in terms of what would have been obtained if high-resolution methods had been used. As noted above, conversion factors of 0.5 and 1.0 have been reported in the literature (*32*), which pertain to packed column results based on about seven or eight peaks. Had we used these factors to reexpress the North Carolina data and accounted for the fewer peaks used in North Carolina, the estimated median concentration of PCB 153 would have been 50 and 100 ng/g, respectively (instead of 80 ng/g). The former value is just above that estimated for the New York study; the latter is the same as that reported for the Québec study. Recalculation of the Michigan results using a conversion factor of 0.5 instead of 1.1 gives a median PCB 153 level of 50 ng/g, which again is just above that estimated for the New York study.

Along similar lines, the reexpression of packed column results was influenced by our choice of the proportion of quantitated PCBs composed of PCB 153. Among those studies that based their calculation of the sum of quantitated PCBs on the sum of more than four congeners measured by high-resolution methods, the median proportion PCB 153 was 0.22 (range, 0.18–0.34), compared with the values of 0.17 and 0.18 used for the North Carolina and Michigan studies, respectively. Recalculation of the results for the latter two studies, using the median and highest reported proportions, yielded median PCB 153 levels of 0.10 and 0.15 for North Carolina and 0.15 and 0.22 for Michigan.

Among the five studies for which we had data on the ratio of PCBs in milk to serum, the median was 1.34 (range, 0.79–1.77). Our estimated serum PCB 153 levels in New York, Massachusetts, and Germany depended on this ratio, so we recalculated the estimated levels for these three studies using the lowest and highest reported ratios. The median values obtained (ng/g lipid) were 70 and 30 for New York, 50 and 20 for Massachusetts, and 230 and 100 for Germany.

Another assumption was that the concentration of serum lipids was 7.9 g/L. This assumption affected results for North Carolina and Michigan. Among the five studies in which serum lipids were measured, the median was 7.9 g/L (range, 7.3–8.9). We examined the effect of using either 7.3 g/L or 8.9 g/L as the lipid level in each of these two studies; the impact on the results was negligible.

We assumed a recovery of 0.60 for PCB 153 to estimate levels for the U.S./11 cities study (*15*) and the Faroe Islands study (*18*). The average recoveries for the four major congeners in that laboratory ranged from 0.60 to 0.72, a 12% span. We used this span to inform our choice of alternate recovery values to use in our sensitivity analyses. Thus, instead of 0.60, we redid the calculations using recovery proportions of 0.55 and 0.65 (reflecting a 10% span); the resulting median PCB 153 values were not substantially different from the values presented in Figure 1 (0.16 and 0.13 for the U.S. study and 0.49 and 0.42 for the Faroes study). Recovery rates in Michigan were not available; if they were lower than 1.0, the PCB levels could have been slightly higher than shown in Figure 1.

The ratio of median PCB 118 to median PCB 153 concentration ranged from 0.14 in the northern Québec study to 0.87 in the U.S./11 cities study (Table 2), reflecting some variation in the relative amounts of congeners present in the different populations, places, and times studied. We used these ratios, in combination with the estimated median PCB 153 levels (Table 3), to estimate the median concentration of PCB 118 in each population. PCB 118 levels were similar across studies, although levels were higher in the Faroes (as before) and were relatively higher in the three earliest studies (data not shown).

**Table 3.** Median PCB 153 serum levels among 10 studies of PCBs and neurodevelopment.

| Reference number | Location of population | Years specimens collected | Median (ng/g lipid) |
|---|---|---|---|
| (*15*)[a] | U.S./11 cities | 1959–1965 | 140 |
| (*16*)[a] | U.S./California | 1964–1967 | 130 |
| (*7*) | U.S./North Carolina | 1978–1982 | 80 |
| (*8*) | U.S./Michigan | 1980–1981 | 120 |
| (*9*) | Netherlands/2 cities | 1990–1992 | 100 |
| (*10*) | U.S./New York | 1991–1994 | 40 |
| (*11*) | Germany/Düsseldorf | 1993–1995 | 140 |
| (*17*)[a] | U.S./Massachusetts | 1993–1998 | 30 |
| (*12*) | Denmark/Faroe Islands | 1994–1995 | 450 |
| (*18*)[a] | Canada/Northern Québec | 1995–1998 | 100 |

PCB 153 serum levels were estimated in some instances (see "Methods").
[a]References for these studies are for initial publications; results for neurodevelopmental outcomes are not yet published.

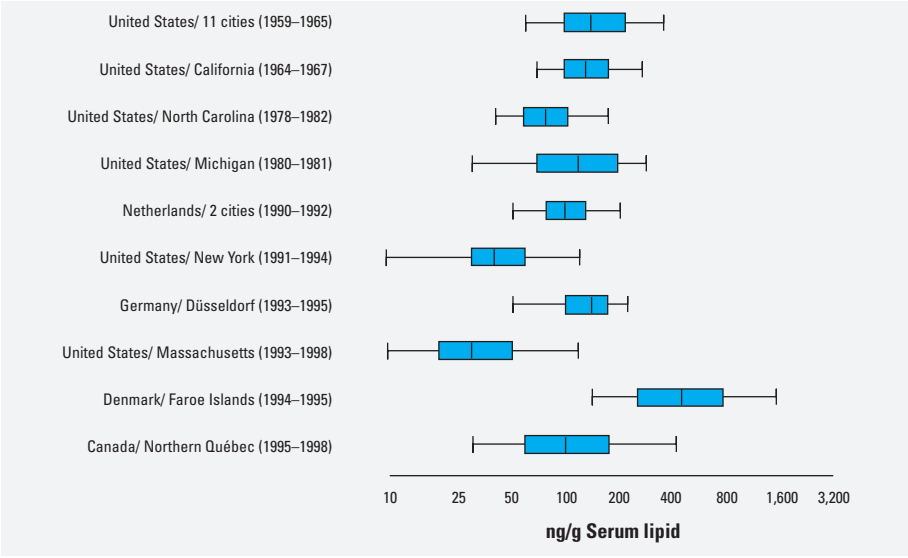


**Figure 1.** Percentiles of the distribution of PCB 153 concentration in serum (5th, 25th, 50th, 75th, and 95th), obtained using methods to express levels in a uniform manner. Data from 10 studies of neurodevelopment in humans.

## Discussion

The primary findings based on the reported or estimated level of PCB 153 were that *a*) the distribution of exposure in the majority of studies overlapped substantially, *b*) exposure levels in the Faroe Islands study was about 3–4-fold higher than in most other studies, and *c*) the exposure levels in the more recent U.S. studies were one-third or more lower than in the earlier U.S. studies or more recent European and northern Québec studies.

The coefficient of variation (CV) for the 10 median PCB 153 levels was 88%. In recent interlaboratory comparisons done by investigators in Germany, with specimens from the same serum pool analyzed by different laboratories using high-resolution methods, the among-laboratory CV for PCB

153 at environmental levels (130 ng/g lipid) was 23% ($n$ = 27 laboratories) and, in another assessment, was 44% at 190 ng/g lipid ($n$ = 29 laboratories) (*33*). In a similar comparison recently done by investigators in the United States, the among-laboratory CV for PCB 153 (250 ng/g lipid) was 12% ($n$ = 6 laboratories) (*34,35*). Thus, the CV among our 10 studies exceeded that expected because of interlaboratory differences, supporting the idea that the exposure levels in the Faroe Islands and the two recent U.S. studies were truly different from the others. If we exclude those three studies and calculate the CV among the remaining seven studies, it is 20%. The similarity of the seven-study CV with that of the among-laboratory CVs suggests that the observed spread in median PCB levels among the seven studies could be due entirely to differences from minor variation in laboratory results, although there is no reason to reject true differences in exposure across populations.

The sensitivity analyses gave some indication of the level of uncertainty about the results. The assumptions with the largest potential effect on the findings for which we have the least confidence were those regarding *a*) reexpression of packed column results as high-resolution results and *b*) the conversion of milk to serum PCB levels. The sensitivity analysis suggests that imprecision introduced by these assumptions, however, would probably not alter our primary findings. We note that in the Dutch study (*9*), for most major PCBs, the ratio of levels in milk and serum was similar to that for PCB 153, suggesting that use of the milk:serum ratio for PCB 153 instead of the sum of quantitated PCBs would not have had an important effect on our findings. We chose not to consider the effect of detection limits being different across studies, because the median levels of PCB 153 (or for the sum of quantitated PCBs in the case of North Carolina or Michigan) were well above such limits in all studies. The precision of the lower 5% bounds of the study-specific distributions of PCB 153 could have been affected by the detection limits and by the investigators' decisions on how to handle values below those limits.

We chose to examine PCB levels expressed on a per-unit-serum-lipid basis, to account for the effect of variation in serum lipid concentrations. Although accounting for lipid levels is sensible, roughly half of serum PCBs are associated with albumin and other proteins that are not lipoproteins (*36,37*). Whether albumin levels vary substantially among pregnant women from different populations is not clear, although it seems likely that variations in lipid concentration would be a greater source of variation in PCBs. We also note that imprecision of the gravimetric assay for milk lipids could contribute to the wide variation in the ratio of milk to serum levels of PCBs, although direct comparisons of enzymatic and gravimetric lipid measures have shown a high level of agreement (*38,39*).

The use of PCB 153 to assess relative levels of exposure across populations has many strengths, such as nearly always being the largest individual component of the total, being fairly well resolved from most coeluting compounds, and being very long-lived in the body. Yet use of PCB 153 to compare exposures among various epidemiologic studies has potential limitations. Although PCB 153 constitutes a major fraction of the total PCBs in humans, its proportion may vary as the source or type of PCB exposure varies across different populations. A detailed assessment of the variation in congener proportions in the 10 studies considered is beyond the scope of the present report. In addition, different sets of congeners were quantitated in each study, further complicating a meaningful comparison of PCB patterns across studies. Besides PCB 153, PCBs 118, 138, and 180 are the major congeners present and are also usually quantitated. The ratio of median PCB 118 level to median PCB 153 level varies more than for the corresponding ratios for 138 to 153 or for 180 to 153 (*7–9,12,15,17,18,20–22,40,41*). This is consistent with the possible greater ease of elimination of the pentachlorobiphenyl PCB 118 compared with the hexachlorobiphenyls PCBs 138 and 153 and the heptachlorobiphenyl PCB 180. When we examined PCB 118 levels across studies (calculated using the 118:153 ratio) to assess the robustness of the 153-based comparison, the results suggested that the 153-based comparison (or any comparison based on the major congeners) works best for those studies that have greater uniformity in the mixture of major congeners present [e.g., (*9,10,11,12,18*) but not (*15*)]. The high correlation among levels of the major specific PCB congeners within subjects in any given background-exposed study population has been well documented (*20–22,42*). If the concentration of PCB congeners responsible for toxicity is proportional to that of PCB 153, the latter is likely to give a useful indication of the relative exposure level across studies.

The data on PCBs and neurodevelopment are not yet published for 4 of the 10 studies included here. Our results are an important first step toward making interpretation of existing and new data on PCB exposure in relation to neurodevelopment more straightforward.

## References and Notes


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