Effect of Prenatal Exposure to Polychlorinated Biphenyls on Incidence of Acute Respiratory Infections in Preschool Inuit Children

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OBJECTIVE: We set out to assess whether environmental prenatal exposure to polychlorinated biphenyls (PCBs) is associated with incidence of acute respiratory infections in preschool Inuit children.

STUDY DESIGN: We reviewed the medical charts of 343 children from 0 to 5 years of age and evaluated the associations between PCB-153 concentration in umbilical cord plasma and the incidence rates of acute otitis media (AOM) and of upper and lower respiratory tract infections (URTIs and LRTIs, respectively).

RESULTS: The incidence rates of AOM and LRTIs were positively associated with prenatal exposure to PCBs. Compared with children in the first quartile of exposure (least exposed), children in fourth quartile (most exposed) had rate ratios of 1.25 ($p < 0.001$) and 1.40 ($p < 0.001$) for AOM and LRTIs, respectively. There was no association between prenatal PCB exposure and incidence rate of URTIs or hospitalization.

CONCLUSION: Prenatal exposure to PCBs could be responsible for a significant portion of respiratory infections in children of this population.

KEY WORDS: cord blood, environmental health, human, infections, Inuit, organochlorines, pesticides, polychlorinated biphenyls, prenatal exposure, respiratory tract infections. Environ Health Perspect 114:1301–1305 (2006). doi:10.1289/ehp.8683 available via http://dx.doi.org/[Online 13 March 2006]

It is well known that Inuit children from Canada, United States, and Greenland suffer from a high incidence of respiratory infections, and many authors have identified higher rates of ear infections and lower respiratory tract infections (LRTIs) in Inuit populations compared with Caucasian populations (Banerji et al. 2001; Bluestone 1998; Curns et al. 2002; Davidson et al. 1994; Holman et al. 2001; Karron et al. 1999; Koch et al. 2002; Ling et al. 1969; Lowther et al. 2000; Wainwright 1996). Among the factors suspected to be involved in this phenomenon, perinatal exposure to persistent organic pollutants has been implicated (Dallaire et al. 2004; Dewailly et al. 2000). The immunotoxic potential of some organochlorine compounds (OCs), such as 2,3,7,8-tetrachlorodibenzop-dioxin (TCDD) and polychlorinated biphenyls (PCBs), is well known (Belles-Isles et al. 2002; Chang et al. 1982; Hoffman et al. 1986; Lu and Wu 1985; Neubert et al. 1992; Tryphonas et al. 1991a, 1991b). Although their production and use are now banned in many countries, a significant proportion of what has been emitted in the environment is still present in the biota of almost every region of the world (Braune et al. 1999; Burke and Kallenborn 2000; Macdonald et al. 2000). The high degree of chlorination of OCs renders them resistant to biodegradation. They accumulate in adipose tissues of living organisms and are biomagnified in the food chain (Evans et al. 1991). The highest plasma concentrations were observed in top predator species (Braune et al. 1999; Muir et al. 1999; Skaaere et al. 2000) and in humans with seafood-rich diets (Bjerregaard et al. 2001; Dewailly et al. 1993; Humphrey et al. 2000; Sjödin et al. 2000).

The Nunavik region is located in the northernmost part of the province of Québec, Canada. Around 9,600 Inuit inhabit 14 Inuit communities spread out on the coastline of Hudson Bay, the Hudson Strait, and the Ungava Bay. For cultural and economical reasons, carnivorous fish and marine mammals constitute an important part of the diet of the Inuit population of Nunavik. Their exposure to food-chain contaminants, such as OCs, is thus proportionally high. Several studies have identified markedly higher concentrations of OCs in adult blood, umbilical cord blood, and breast milk of Nunavik inhabitants, compared with those of the mostly Caucasian southern Québec population (Ayotte et al. 1997, 2003; Dewailly et al. 1993; Muckle et al. 1998, 2001b; Rhaïns et al. 1999).

In 2000, we published a first study showing an association between perinatal exposure to OCs and acute otitis media (AOM) in Nunavik Inuit infants (Dewailly et al. 2000). To further document this association, we investigated the relation between maternal OC concentrations and acute respiratory and gastrointestinal infections in a second cohort of 199 infants of the same population (Dallaire et al. 2004). We found that OC concentrations in maternal plasma were positively associated with incidence of acute infections during the first 6 months of life, but not afterward. The number of subjects was small, however, and the associations were not always statistically significant. To clarify the possible link between prenatal exposure to OCs and infections in this population, we report here the association between PCB-153 concentrations in umbilical cord blood and incidence rate of acute respiratory tract infections in a third cohort of 343 preschool children of Nunavik born between 1993 and 1996.

Materials and Methods

Study population. Between 1993 and 1996, we monitored the concentrations of OCs and heavy metals in umbilical cord blood of Nunavik newborns (Dewailly et al. 1998). Four hundred ninety-one unselected pregnant women from the 14 Inuit communities of Nunavik were enrolled in the study. The women were invited to participate at their arrival at one of the two health centers in Nunavik for delivery (Puvirnituq and Kuujjuaq). Women giving birth elsewhere were not included. A sample of cord blood was taken, and an interview was conducted with the mothers 1–4 weeks after delivery. When we initiated the present study, children born to these mothers were between 5 and 7 years of age. They were the targeted participants for the present study. The study protocol was reviewed and approved by the Nunavik Health and Nutrition Committee and by the ethics committee of Laval University. All participants gave written informed consent before the study.

Medical chart review and interview. We attempted to locate and review the medical charts of all the children included in the cord blood monitoring program mentioned above. Five second- and third-year trained medical students reviewed the charts using a standardized questionnaire. For every diagnosis of...
infection noted in the charts, we recorded the date of diagnosis, whether antibiotics were prescribed, and whether the child was hospitalized. For each infection, we also attributed a date of diagnosis, whether antibiotics were used. Infections noted in the charts, we recorded the date of diagnosis, whether antibiotics were used.

Dallaire et al. selected chlorinated pesticides and their metabolites: one in which exposure to PCB-153 was the most abundant congener, and its concentration is strongly correlated with all the moderate to highly chlorinated PCB congeners and with most chlorinated pesticides. For these reasons, it has been shown to be a good marker of exposure to most OCs in the Arctic aquatic food chain (Muckle et al. 2001b). Participants were grouped according to their quartile of PCB-153 concentrations in cord blood. Children in the lowest quartile were used as the group of reference.

Statistical analyses. Contaminant concentrations had lognormal distributions and were log-transformed in all analyses. Therefore, contaminants results are presented as geometric means. We used Poisson regression to evaluate incidence rate ratios (IRR) comparing the number of diagnosed and reported infections during the first 3 years of life as the dependent variable and PCB-153 concentration in cord blood as the independent variable. For every analysis, we constructed two models: one in which exposure to PCB-153 was considered as a continuous variable and PCB-153 concentration in cord blood as the main independent variable. For every analysis, we constructed two models: one in which exposure to PCB-153 was considered as a continuous variable and PCB-153 concentration in cord blood as the main independent variable. For every analysis, we constructed two models: one in which exposure to PCB-153 was considered as a continuous variable and PCB-153 concentration in cord blood as the main independent variable.

Results

Participants. Four hundred ninety-one women were included in the initial cord blood monitoring program. Fifty children were initially excluded because contaminant concentrations were not available or because there was not enough information in our database to trace the charts. Of the 441 remaining participants, it was impossible to get the chart of 43 (9.8%) children for various logistical reasons. Among the 398 available charts, 28 (7.0%) were incomplete, 17 (4.3%) families moved out of Nunavik during follow-up, 7 (1.8%) children died, and 3 (0.8%) children were excluded because they suffered from a serious chronic disease. The final analyses included the 343 remaining children. Table 1 shows the characteristics for all participants.

Contaminant concentrations. Detailed contaminant concentrations in cord blood for these children have been published elsewhere (Dewailly et al. 1998). On a lipid basis, the geometric mean concentration of the sum of the 14 PCB congeners (ΣPCBs) in cord blood included in the final adjusted model were maternal age (10-year categories) and parity (categories). The variables included were smoking during pregnancy (yes/no), sex of the child, reviewer of the medical chart, and gestational age (preterm/term). Vaccination coverage was considered as a potential confounding factor, but the information on vaccination gathered through the review of the medical chart was inconsistent. Because preliminary analyses showed that vaccination coverage was not related to contaminant burden, and because we found no scientific report linking vaccination coverage with OC exposure, we excluded it from the final analyses.

We used SPSS Data Entry Builder (version 2.0; SPSS Inc., Chicago, IL, USA) for data entry and SAS (version 8.02; SAS Institute Inc., Cary, NC, USA) for database management and statistical analyses. A p-value < 0.05 was considered significant.

Table 1. Characteristics of participants (n = 343).

| Characteristic       | Value |
|----------------------|-------|
| Children             |       |
| Male sex (%)         | 49.0  |
| Year of birth (%)    |       |
| 1984                 | 37.3  |
| 1995                 | 32.1  |
| 1996                 | 30.6  |
| Hospital of delivery |       |
| Puvirnituq           | 48.7  |
| Kuujjuarjuaq         | 51.3  |
| Gestational age (weeks) |   |
| Mean gestational age | 39.1  |
| Preterm (< 37 weeks) | 5.3   |
| Birth weight (mean [g]) | 3,494 |
| Length (mean [cm])   | 51.5  |
| Mothers              |       |
| Age (mean [years])   | 23.7  |
| Parity (mean)        | 2.1   |
Table 3. Incidence RR of AOM, URTIs, and LRTIs according to prenatal exposure to PCB-153.

| Prenatal exposure model | RR (95% CI) | AOM | URTIs | LRTIs |
|-------------------------|------------|-----|-------|-------|
| Unadjusted model (n = 330) |             |     |       |       |
| Continuous (for each log increase) | 1.065 (1.002–1.131)* | 0.943 (0.887–1.002) | 1.109 (1.019–1.208)* |
| Categories* |            |     |       |       |
| Q1 (least exposed) | 1.00 (referent) | 1.00 (referent) | 1.00 (referent) |
| Q2 | 1.13 (1.00–1.28)* | 0.96 (0.86–1.08) | 1.37 (1.15–1.63)* |
| Q3 | 1.18 (1.04–1.33)* | 0.90 (0.80–1.02) | 1.21 (1.01–1.44)* |
| Q4 (most exposed) | 1.25 (1.10–1.41)* | 1.00 (0.99–1.12) | 1.40 (1.18–1.67)* |
| Adjusted model (n = 330) |             |     |       |       |
| Continuous (for each log increase) | 1.123 (1.052–1.189)* | 0.995 (0.931–1.063) | 1.135 (1.036–1.243)* |
| Categories* |            |     |       |       |
| Q1 (least exposed) | 1.00 (referent) | 1.00 (referent) | 1.00 (referent) |
| Q2 | 1.15 (1.01–1.31)* | 0.99 (0.87–1.12) | 1.39 (1.16–1.66)* |
| Q3 | 1.26 (1.11–1.43)* | 0.95 (0.83–1.07) | 1.25 (1.04–1.50)* |
| Q4 (most exposed) | 1.37 (1.20–1.55)* | 1.09 (0.97–1.24) | 1.44 (1.20–1.72)* |

CI, confidence interval.
*Quartiles of PCB-153 concentration in cord blood. *p < 0.05.
more closely associated with infection incidence rates compared with PCB-153 concentration (Dallaire et al. 2004). In the present study, results for DDE exposure are not presented but were in general similar to those for PCB-153. Although our analyses were conducted using PCB-153 as a proxy for OC exposure, the potential harmful effect on the immune system could be attributed to other compounds highly correlated to PCB-153 concentration.

The associations shown in this study were estimated using prenatal exposure only. Although the immune system is most vulnerable during its development in utero, postnatal exposure to the same compounds through breast-feeding and food consumption could also increase susceptibility to infections. It is likely that prenatal and postnatal exposures were correlated because eating habits of a mother will probably influence her child’s diet. It is therefore possible that part of the association with prenatal exposure was actually due to postnatal exposure.

In this study, we used a review of the medical charts to evaluate incidence rates. There is only one health center in each community included in this study. Participants almost always visit that health center when they seek medical attention, and copies of consultations done elsewhere are routinely requested to complete medical charts. We are therefore confident that we have reviewed most outpatient visits sought by the participants. Nevertheless, we did not attempt to verify every diagnosis, nor did we try to inquire about infections for which medical attention was not sought by the parents. It is therefore important to keep in mind that the incidence rates reported here are underestimated. We cannot exclude the possibility that the propensity to seek medical attention when respiratory symptoms are present was associated with traditional lifestyle, which in turn is known to be associated with OC concentration in maternal blood (Muckle et al. 2001a). Should this happen with our participants, the direction of the bias that would be introduced would be unknown. We find it improbable, however, that Inuit families with a traditional lifestyle would increase their frequency of medical contacts in such a way that the full extent of the observed association would be solely due to this bias, if any.

Inuit children from Nunavik are burdened by a high rate of respiratory infectious diseases. In a related study on infection incidence conducted with the same cohort, we showed that LRTIs are far more frequent in Nunavik compared with other Canadian populations and that the hospitalization rate for LRTIs in Nunavik was one of the highest ever reported in recent scientific literature (Dallaire et al., in press). If the association between respiratory infection and prenatal exposure to PCBs observed in this population is causal, exposure to PCBs during development would be responsible for a clinically significant proportion of respiratory infectious episodes in these children. The biologic mechanism of this effect in humans environmentally exposed is still obscure. Other studies are needed to identify which immune pathways are affected in exposed children.

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