The Inuit population of Nunavik (Canada) is exposed to immunotoxic organochlorines (OCs) mainly through the consumption of fish and marine mammal fat. We investigated the effect of perinatal exposure to polychlorinated biphenyls (PCBs) and dichlorodiphenyltrichloroethene (DDE) on the incidence of acute infections in Inuit infants. We reviewed the medical charts of a cohort of 199 Inuit infants during the first 12 months of life and evaluated the incidence rates of upper and lower respiratory tract infections (URTIs and LRTIs, respectively), otitis media, and gastrointestinal (GI) infections. Maternal plasma during delivery and infant plasma at 7 months of age were sampled and assayed for PCBs and DDE. Compared to rates for infants in the first quartile of exposure to PCBs (least exposed), adjusted rate ratios for infants in higher quartiles ranged between 1.09 and 1.32 for URTIs, 0.99 and 1.39 for otitis, 1.52 and 1.89 for GI infections, and 1.16 and 1.68 for LRTIs during the first 6 months of follow-up. For all infections combined, the rate ratios ranged from 1.17 to 1.27. The effect size was similar for DDE exposure but was lower for the full 12-month follow-up. Globally, most rate ratios were > 1.0, but few were statistically significant (p < 0.05). No association was found when postnatal exposure was considered. These results show a possible association between prenatal exposure to OCs and acute infections early in life in this Inuit population.

Key words: cord blood, environmental health, gastrointestinal infections, human, infant, infections, Inuit, organochlorines, otitis, pesticides, polychlorinated biphenyls, prenatal exposure, respiratory tract infections. Environ Health Perspect 112:1359–1364 (2004). doi:10.1289/ehp.7255 available via http://dx.doi.org/ [Online 18 August 2004]
study were Inuit infants born in Puvirnituq, Inukjuak, and Kuujjuarapik, the three largest Inuit communities on the Hudson Bay coast in Nunavik. The recruitment procedures have been described elsewhere (Muckle et al. 2001). Briefly, between November 1995 and March 2001, we attempted to contact every pregnant woman after their first prenatal medical visit either by phone or by the community radio (for those without a telephone at home). Pregnant women were invited to meet with our research assistant, and women willing to participate were asked to sign an informed consent form. The study was part of a larger study focusing on environmental contaminants and neurobehavioral development. The study protocol was reviewed and approved by the Nunavik Health and Nutrition Committee and by the ethics committee of Laval University.

Data collection and biological sampling. In order to gather biological samples and information on confounding variables, we conducted four interviews: one at midpregnancy (prenatal interview, median of 21 weeks gestation) and three with the infant and the mother at 1, 6, and 11 months postpartum. We collected information on maternal age, breast-feeding duration, socioeconomic status of the caregiver (Hollingshead index), smoking habits during pregnancy, environmental tobacco exposure during the first year of life, number of children living with the participant, village of residence, and day care attendance. Many other characteristics were also documented for the neurobehavioral arm of this cohort but were not included in this study.

We sampled maternal blood at delivery or, when it was impossible, as soon as possible after delivery (median, 2 days postpartum). We also obtained umbilical cord blood at delivery and infant blood at midfollow-up (median, 7.0 months of age). All blood samples were immediately centrifuged and frozen at −80°C. Frozen blood and plasma samples were sent to the Centre de Toxicologie (Institut National de Santé Publique du Québec, Québec City, Canada) every 3–6 months for contaminants and biochemical analyses. Finally, we extensively reviewed the medical charts of the mother and the infant for the pregnancy period and for the infant’s first year of life.

Determination of OCs. We determined the concentrations of p,p’-dichlorodiphenyl-dichloroethylene (DDE) and 14 PCB congeners (International Union of Pure and Applied Chemistry numbers 28, 52, 99, 101, 105, 118, 128, 138, 153, 156, 167, 180, 183, and 187) in plasma samples by high-resolution gas chromatography. OCs were extracted from plasma with ammonium sulfate:hexane (1:1:3). The extracts were cleaned on florisil columns, taken to a final volume of 100 µL, and analyzed on an HP-5890 series II gas chromatograph equipped with dual-capillary columns and dual Ni-63 electron capture detectors (Hewlett-Packard, Palo Alto, CA, USA). We identified peaks by their relative retention times obtained on the two columns. Quality control procedures were described previously (Rhaïms et al. 1999). Percent recovery ranged from 89 to 100%, and the detection limit was approximately 0.02 µg/L for all compounds. Coefficients of variation (n = 20, different days) ranged from 2.1 to 9.1%. The difference between the concentration of reference material and that of the enzymatic method of Takayama et al. (1977) was 10.9 to 3.8%. Because OCs are stored mainly in body fat, all results for contaminants are estimated using plasma concentration of OCs in infant blood at 7 months of age. The concentration of OCs in blood is well correlated with that found in adipose tissues, and it has been shown that either blood or adipose tissue concentrations are valid exposure measurements in epidemiologic studies (Dewailly et al. 1994).

We used PCB-153 concentration (log-transformed) as a surrogate measure for the total PCB burden. PCB-153 is the most abundant PCB congener. Its concentration is strongly correlated with all the moderate-to-heavy chlorinated congeners and with most chlorinated pesticides (except p,p’-DDT). It has been shown to be a good marker of exposure to most organochlorines in the Arctic (Muckle et al. 2001).

Medical chart review and incidence of infectious diseases. Trained research nurses used a standardized questionnaire to review the medical charts of infants for the first 12 months of life. For every diagnosed health problem, we noted the date of diagnosis and the duration of hospitalization (if hospitalized). We also attributed a code corresponding to the International Classification of Primary Care, 2nd edition (ICPC-2; World Organization of National Colleges, Academies and Academic Associations of General Practitioners 1998). We then formed four groups of infections: upper respiratory tract infections (URTIs), otitis media, gastrointestinal (GI) infections, and lower respiratory tract infections (LRTIs). We also added a fifth group labeled “all infections,” which included all of the four preceding groups. Because previous studies on OCs and infections in children seem to point toward a greater association between OCs and otitis media compared with other infectious diseases, we excluded ear infections from the URTI category so that otitis and URTIs could be analyzed independently (Chao et al. 1997; Dewailly et al. 2000; Weisglas-Kuperus et al. 2000). The URTI category included streptococcal pharyngitis and tonsillitis, acute upper respiratory tract infection not otherwise specified (NOS), acute rhinitis, head cold, nasopharyngitis, pharyngitis, and coryza. The otitis category included acute suppurative otitis media, otitis media NOS, acute tympanitis, otitis media with effusion, serous otitis media, and glue ear. The LRTI category included acute bronchitis and bronchiolitis, acute lower respiratory tract infection NOS, chest infection NOS, laryngotracheobronchitis, tracheobronchitis, bacterial and viral pneumonia, bronchopneumonia, influenza pneumonia, and pneumonitis. The GI infection category included GI infection and dysentery with specified organism, diarrhea or vomiting presumed to be infective, dysentery NOS, and gastric flu.

For every health problem identified, we trusted the diagnosis of the attending physician.
When two physicians disagreed, we only recorded the last diagnosis made. In some Inuit communities, nurses are trained to identify and treat benign infections, especially otitis media and URTIs. When the child was not seen by a physician, we recorded the diagnosis of the nurse. We considered two episodes of the same infection type to be separate when there was at least 15 days between the two diagnoses and when it was not specified in the chart that the second episode was related to the first. When an episode of URTI led to a LRTI, we only included the latter in the analysis. We did not attempt to investigate infectious episodes for which treatment at the health center was not sought by the parents. Data on complications or abnormal events during pregnancy, infant sex, and birth weight were also gathered from the medical charts.

Statistical analyses. We assigned a value of one-half the detection limit of the analytical method when a compound was not detected in a sample. OC concentrations had log-normal distributions and were log-transformed in all analyses. Therefore, results for contaminants are presented as geometric means. The correlation between contaminant concentrations was evaluated using Pearson’s method on log-transformed values. To evaluate associations between OC exposure and infection incidence rates, we used Poisson regression with quartiles of OC concentration as the main independent variable, and individual incidence rates as the dependent variable (both for bivariate and multivariate analyses). We categorized the exposure using quartiles boundaries, with the first quartile as the group of reference (Table 1). Regression results are, therefore, an estimate of the incidence rate ratios (RRs) for infants in the three highest quartiles of exposure, when infants in each of these quartiles are compared to infants in first quartile. To test the hypothesis of a dose–response association between incidence rates and OC concentrations (p-value for trend), we included the contaminant concentration (log-transformed) directly in the model and treated it as a continuous variable.

We based the selection of potential confounding variables on clinical knowledge and a literature review. Every identified potential confounding variable was tested in the model, but only those influencing the incidence rate ratios by > 5% were included in the final model. The variables initially excluded from the model were retested one by one in the final model to ensure that their exclusion did not influence the results. The variables included in the final model were maternal age at delivery (continuous), season of birth, year of birth (category), breastfeeding duration (categories), sex of the infant, socioeconomic status of the caregiver (continuous), smoking during pregnancy (yes/no), number of cigarettes smoked per day during pregnancy (continuous), number of children < 6 years of age living with the infant (continuous), and village of residence. The following variables were excluded from the final model because they did not significantly affect the association of interest: day care frequeentation (ever/never), mean hours per week in day care (continuous), maternal omega-3 fatty-acid concentration in blood (continuous), proportion of omega-3 highly unsaturated fatty acids (continuous), number of smokers in the house where the infant resided (continuous), birth weight, gestational age, and reviewer of the medical chart. When postnatal exposure was investigated, we included in the model the infant’s age when the blood sample was drawn. We considered vaccination coverage a potential confounding factor. Information on vaccination was gathered through the review of the medical charts, but information was missing for many children. Preliminary analyses showed that vaccination coverage was not related to contaminant burden. We thus excluded it from the final models.

All modeling results are presented for both the crude model (only exposure categories) and the adjusted model (exposure categories and all the confounding variables mentioned above). Statistical analyses and database management were conducted using the SAS system 8.02 (SAS Institute, Cary, NC, USA). By convention, a p-value < 0.05 was considered significant.

Results

Recruitment and participation. During the study period, 417 pregnancies were identified in the targeted communities. Of them, we excluded 47 pregnant women (11.3%) who had already been enrolled in the study during a previous pregnancy and 3 women (0.7%) due to miscarriage, and we were unable to contact 9 women (2.2%). Of the 358 eligible women asked to participate, 110 (30.7%) refused. This refusal rate is comparable with that of other prospective studies with several interviews in populations of low socioeconomic status. Of the 248 women willing to participate, we were unable to review the medical charts of 43 infants for the following reasons: 10 (4.0%) moved to another village, 14 (5.6%) were adopted in another village, 11 (4.4%) because of miscarriage or perinatal mortality, and 8 (3.2%) because the mother withdrew from the study. Finally, we excluded 6 (2.4%) participants because no biological samples were available for exposure analysis. A total of 199 participants were included in the final analyses.

Population characteristics. Mothers included in the analysis were mostly from Puvirnituq (45.4%) and Inukjuak (39.3%). The mean age at delivery was 25.2 years, and most of them smoked during pregnancy (91.4% reported smoking at least 1 cigarette/day; mean, 10.6 cigarettes/day). Only 2.6% of the infants were not exposed to second-hand smoke during their first year of life. The mean parity was 2.1. There were more males than females (57.6%), and the mean birth weight and length were 3.454 g and 50.3 cm, respectively. Breast-feeding was very common, and only 12.2% were not breast-fed (most of them because they were adopted).

Incidence of infections. Incidence proportions and rates for selected infections are shown in Table 2. Otitis media was the most frequent infection diagnosed, with a mean of 2.8 episodes per infant-year, followed by URTIs, with 2.4 episodes per infant-year. During the first year of life, almost all infants had at least one episode of otitis (96.0%), and 17.1% had five or more. LRTIs required hospitalization in 31.4% of cases. More than half of the infants (56.8%) were hospitalized at least once during their first year of life.

Contaminant burden in plasma. Table 1 shows the concentration of contaminants in maternal and infant plasma. The geometric

| Contaminant | Percent detected | Geometric mean (95% CI) | Range | Quartile boundaries |
|-------------|------------------|-------------------------|-------|--------------------|
|             |                  |                         |       | 1st                | 2nd         | 3rd         | 4th         |
| Maternal plasma (n = 199) |                  |                         |       | 190–296           | 296–500     | >500        |
| ΣPCBs       | NA               | 308 (279–340)           | 59.6–1.951 | <190               | 190–296     | 296–500     | >500        |
| PCB-153     | 100              | 102 (91.4–113)          | 14.6–709  | <57.6             | 57.6–98.4   | 98.4–170    | >170        |
| DDE         | 100              | 294 (267–324)           | 54.3–2.269 | <183               | 183–281     | 281–472     | >472        |
| Infant plasma (n = 172) |                  |                         |       | 99.0–283           | 283–609     | >699        |
| ΣPCBs       | NA               | 259 (218–307)           | 26.9–3.801 | <99.0         | 99.0–283    | 283–609     | >699        |
| PCB-153     | 96.5             | 78.1 (62.4–92.9)        | ND–1,441 | <28.0             | 28.0–95.3   | 95.3–199    | >199        |
| DDE         | 100              | 256 (214–307)           | 15.6–4.386 | <100            | 100–255     | 255–618     | >618        |

Abbreviations: CI, confidence interval; NA, not applicable; ND, not detected.

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mean concentration of the sum of the 14 PCB congeners (ΣPCBs) in maternal plasma was 308 µg/kg (range, 60–1,951 µg/kg). The concentration of the ΣPCBs was highly correlated with that of PCB-153 in maternal plasma (r = 0.99). The correlation between cord plasma and maternal plasma was also very high, both for the ΣPCBs and for PCB-153 (r = 0.95 and 0.94, respectively). The geometric mean concentration for DDE in maternal plasma was 294 µg/kg (range, 54–2,269 µg/kg). The correlation between cord and maternal plasma samples for DDE was also very strong (r = 0.94). Mean concentrations of PCBs and DDE were lower in infant plasma compared to those in maternal plasma.

**Prenatal exposure to PCB-153 and infections.** The association between prenatal exposure to PCB-153 and incidence of infections is shown in Table 3. In preliminary analyses we found that the associations between OCs and incidence rates were somewhat stronger during the first 6 months of life. Although this study was designed for a 12-month follow-up, we also present the results for the first 6 months of life. Regarding infections during the first 6 months of life and prenatal exposure to PCBs, we observed statistically significant associations only for LRTIs (3rd quartile; RR = 1.54 and 1.68 for the unadjusted and adjusted models, respectively). Although not statistically significant, almost all other RRs detected significant associations with otitis (RR = 1.63, 3rd quartile) and LRTIs (RR = 1.52, 2nd quartile) in the unadjusted model, and with URTIs (RR = 1.56, 2nd quartile) and otitis (RR = 1.83, 3rd quartile) in the adjusted model. The trend was significant for otitis in the unadjusted model (p = 0.04) and borderline significant in adjusted model (p = 0.07). When the four types of infections were combined, we observed significant associations for the 2nd quartile (RR = 1.49 in the unadjusted model, and for the 2nd quartile (RR = 1.38) and 3rd quartile (RR = 1.33) quartiles in the adjusted model. As observed for PCB exposure, almost all RRs were above the unity. When considering the first 12 months of life, we observed significant associations for GI infections (RR = 1.49, 2nd quartile) in the unadjusted model, and for URTIs (RR = 1.34, 2nd quartile) and GI infections (RR = 1.59, 2nd quartile) in the adjusted model. For all infections combined, the association reached statistical significance only for the 2nd quartile in the unadjusted model (RR = 1.17).

**Postnatal exposure to OCs and infections.** We used OC concentrations in infant plasma to evaluate the effect of postnatal exposure on incidence of infections (sampling done at a median age of 7.0 months). We observed no association between postnatal exposure and the incidence of infections (data not shown). The only significant association was for PCBs (12-month follow-up, 2nd quartile, RR = 1.19) in the unadjusted model, but the statistical significance was lost when adjustment for confounding was done.

**Effects of exposure to OCs on hospitalization rate.** We found no significant association between prenatal or postnatal exposure and incidence rate of hospitalization for LRTIs (data not shown). However, statistical power was poor because of the limited number of admissions.

**Discussion**

Accidental and occupational exposure to PCBs has already been associated with increased susceptibility to infections in infants. Rogan et al. (1988) observed that mothers who were exposed to PCBs through the consumption of contaminated rice oil (Yu-Cheng) reported a higher rate of bronchitis in their children than did control mothers. After examination by two otorhinolaryngologists, the same children were also shown to have a higher prevalence of middle ear diseases than matched controls (Chao et al. 1997). In Japan, Hara (1985) noted that infants born to women who had handled PCBs in a capacitor factory had a higher incidence of colds and GI complaints.

### Table 2. Incidence proportion and mean infection incidence rate for all participants (n = 199).

| Infection               | Mean incidence (episodes per person per year) | Percentage of episodes requiring hospitalization | Percentage of participants who had at least 1 episode | 3 episodes | 5 episodes |
|-------------------------|---------------------------------------------|-----------------------------------------------|---------------------------------|------------|------------|
| URTIs                   | 2.4 ± 1.7                                   | 1.3                                           | 90.0                            | 42.7       | 12.6       |
| Otitis media            | 2.8 ± 1.7                                   | 0.9                                           | 96.0                            | 52.8       | 17.1       |
| GI infections           | 1.0 ± 1.1                                   | 3.4                                           | 58.8                            | 10.6       | 0.5        |
| LRTIs                   | 1.7 ± 1.7                                   | 31.4                                          | 73.4                            | 26.6       | 5.5        |

### Table 3. Incidence RR of each PCB-153 quartile of prenatal exposure compared to the first quartile.

| Infection type | Unadjusted (n = 199) | Adjusted (n = 177) |
|----------------|----------------------|---------------------|
|                | 2nd quartile | 3rd quartile | 4th quartile | p-Value for trend | 2nd quartile | 3rd quartile | 4th quartile | p-Value for trend |
| 6-Month follow-up |          |            |            |                  |          |            |            |                  |
| URTIs          | 1.08 (0.76–1.55) | 0.98 (0.69–1.14) | 1.19 (0.84–1.68) | 0.17 | 1.08 (0.69–1.67) | 1.08 (0.71–1.65) | 1.32 (0.87–2.00) | 0.22 |
| Otitis media   | 1.33 (0.85–2.07) | 1.15 (0.73–1.82) | 1.30 (0.83–2.02) | 0.19 | 1.11 (0.65–1.89) | 0.99 (0.59–1.66) | 1.39 (0.82–2.35) | 0.17 |
| GI infections  | 1.63 (0.80–3.34) | 1.31 (0.62–2.76) | 1.55 (0.75–3.20) | 0.33 | 1.89 (0.78–4.56) | 1.52 (0.65–3.54) | 1.54 (0.64–3.60) | 0.38 |
| LRTIs          | 1.12 (0.71–1.76) | 1.54 (1.01–2.35) | 1.01 (0.63–1.61) | 0.61 | 1.16 (0.65–2.09) | 1.68 (1.00–2.81) | 1.18 (0.68–2.04) | 0.38 |
| All infections† | 1.19 (0.95–1.50) | 1.18 (0.94–1.48) | 1.19 (0.95–1.50) | 0.14 | 1.17 (0.88–1.55) | 1.19 (0.92–1.54) | 1.27 (0.88–1.66) | 0.04* |

| 12-Month follow-up |          |            |            |                  |          |            |            |                  |
| URTIs          | 0.93 (0.72–1.20) | 0.87 (0.67–1.13) | 1.12 (0.88–1.43) | 0.81 | 0.99 (0.71–1.36) | 0.96 (0.71–1.29) | 1.23 (0.92–1.65) | 0.29 |
| Otitis media   | 1.05 (0.83–1.32) | 0.97 (0.76–1.22) | 0.94 (0.75–2.0) | 0.89 | 1.02 (0.77–1.35) | 0.89 (0.68–1.17) | 0.97 (0.73–1.28) | 0.89 |
| GI infections  | 1.27 (0.86–1.88) | 1.22 (0.82–1.82) | 1.05 (0.63–1.58) | 0.61 | 1.53 (0.94–2.49) | 1.59 (1.01–2.49) | 1.26 (0.78–2.04) | 0.29 |
| LRTIs          | 0.88 (0.65–1.19) | 1.08 (0.81–1.45) | 0.96 (0.71–1.29) | 0.48 | 0.86 (0.57–1.28) | 1.10 (0.78–1.55) | 1.03 (0.72–1.48) | 0.36 |
| All infections† | 1.00 (0.67–1.15) | 0.99 (0.86–1.14) | 1.01 (0.88–1.16) | 0.67 | 1.02 (0.88–1.21) | 1.01 (0.86–1.19) | 1.08 (0.82–1.29) | 0.24 |

CI, confidence interval.

*Model included mother’s age, season of birth, year of birth, breast-feeding duration, socioeconomic status of the caregiver, tobacco use during pregnancy, village of residence, and number of children living with the participant. #Incidence RR when the given quartile was compared to the first quartile of exposure (Poisson regression). p-Values for trends were calculated by Poisson regression in which the contaminant concentration (lipid-based) was entered as a continuous variable (log-transformed). †Only infections with a mean incidence > 1.0 episode/year/infant were included; see details in “Materials and Methods”.* p < 0.05.
However, evidence of an effect of environmental OC exposure on susceptibility to infections in children is scarce and inconsistent. To our knowledge, the first study addressing this question was conducted in the Great Lakes area (Smith 1984); the author observed that fish consumption during pregnancy (a proxy of PCB exposure) was positively associated with colds, earaches, and flu symptoms in infants. Rogan et al. (1987) followed 900 families in North Carolina (USA) between 1978 and 1982. They reviewed children’s medical charts and did not find any evidence of harmful effects of PCBs or DDE during the first year of life. In the Netherlands, Weisglas-Kuperus et al. (1995) observed no association between PCBs and number of episodes of rhinitis, bronchitis, tonsillitis, and otitis during the first 18 months of life. However, in the same group of children at 42 months of age, current PCB burden was associated with a higher prevalence of recurrent middle ear infections and chicken pox (Weisglas-Kuperus et al. 2000). Karmas et al. (2001) also observed a higher risk of otitis media, but the association was only present with the combined exposure to DDE and PCBs. Finally, our laboratory previously reported that exposed Inuit infants had a higher risk of acute otitis media during the first year of life (third tertile of exposure compared to the first) (Dewailly et al. 2000). The association was significant with exposure to DDE and HCB but remained above the unity for PCBs, dieldrin, and mirex.

In this study, we showed that prenatal exposure to some environmental OC contaminants was possibly associated with a higher incidence rate of infections during the first 6 months of life. Although the associations were not always statistically significant because of limited statistical power, infants in the highest quartiles of PCB and DDE exposure had systematically more episodes of infections than their counterparts in the first quartile of exposure. This was mostly observed during the first 6 months of life, as the effect size was lower when infections during the first 12 months of life were considered. Postnatal exposure to OCs was not associated with infection incidence.

In the literature, middle ear infections are the most consistently reported infections associated with prenatal exposure to OCs. In our study, the strongest dose–response relationship was seen with ear infections. However, it is likely that insults of OCs on the developing immune system would result in the increase of incidence of many different types of acute infections and not only ear infections. Consistent with that assumption, our results showed a higher incidence rate for the four most frequent infections in infants in the higher exposure groups, and the rate ratios were similar to that observed for otitis. Furthermore, when these four types of infections were combined, the association was more stable and the magnitude of the dose–response relationship was increased, compared with that of the four types of infection taken separately.

We also observed that the effect of prenatal exposure was mostly present during the first few months of life and that this effect seemed to vanish after 6 months of life. Furthermore, we found no effect of postnatal exposure to OCs with infections. It has already been suggested that the immune system is vulnerable to immunotoxic compounds during its development and that high maternal burden during pregnancy and lactation could lead to permanent defects on the infant’s immune system (Badessa et al. 1995; Barnett et al. 1987). Our results support the hypothesis of a stronger effect during early infancy, but we were unable to clearly identify any harmful effect persisting after the age of 6 months. After a few months of life, cumulative environmental influences on the immune system may begin to play a larger role, thus increasing the variability of responses to infections. Furthermore, contributions of the OC exposure via breast milk, entangled with the beneficial effect of breastfeeding on infections, might have masked the effect. This could explain in part the discrepancies in results of other studies on OCs and infections because the age of children during disease and exposure assessment varied considerably between studies. Further studies are needed to clarify the time period during which environmental exposure to OCs has a detrimental effect on children’s health.

In this population, plasma concentrations of many environmentally persistent OCs are strongly correlated (Muckle et al. 2001). Muckle et al. (2001) also showed that concentrations in cord plasma, maternal plasma, and breast milk samples are also strongly correlated. With such exposure, it is therefore not possible to attribute the effect observed to one specific OC compound, nor are we able to unravel the specific contribution of PCB-153 exposure from DDE exposure. Furthermore, our data did not allow us to determine whether the association between DDE and infections was due to an immune modulation property of DDE, to co-linearity with PCB-153, or both.

We used a review of the medical charts to evaluate disease frequency. There is only one health center in each of the three Inuit communities included in this study, and participants almost always go to that health center when they seek medical attention; copies of consultations performed elsewhere are routinely requested to complete medical charts. We are therefore confident that we have reviewed a majority of the medical consultations sought by the participants. Nevertheless, we did not attempt to verify every diagnosis, nor did we try to inquire about infections for which we did not attempt to verify every diagnosis.

### Table 4. Incidence RR of each DDE quartile of prenatal exposure compared to the first quartile

| Infection type | 2nd quartile (n = 40) | 3rd quartile (n = 46) | 4th quartile (n = 45) | p-Value for trend |
|----------------|----------------------|----------------------|----------------------|------------------|
| Unadjusted (n = 199) | Adjusted (n = 177)* |
| URIs | 1.50 (1.05–2.13) | 1.56 (1.05–2.33)* | 1.15 (0.75–1.75) | 0.91 |
| Otitis media | 1.27 (0.79–2.05) | 1.03 (0.59–1.77) | 1.83 (1.09–3.07)* | 0.04* |
| GI infections | 2.16 (1.02–4.55)* | 1.91 (0.84–4.35) | 1.66 (0.69–3.97) | 0.34 |
| LRTIs | 1.52 (1.00–2.32)* | 1.40 (0.86–2.29) | 1.22 (0.72–2.05) | 0.75 |
| All infections | 1.49 (1.19–1.87)* | 1.38 (0.87–1.78)* | 1.33 (1.03–1.97)* | 0.22 |
| 6-Month follow-up | 1.34 (1.00–1.78)* | 1.30 (0.96–1.78) | 0.98 |
| URIs | 1.51 (1.00–2.32)* | 1.09 (0.81–1.47) | 1.00 (0.83–1.28) | 0.39 |
| Otitis media | 1.00 (0.79–1.27) | 0.89 (0.68–1.17) | 1.02 (0.76–1.35) | 0.36 |
| GI infections | 1.49 (1.00–2.32)* | 1.09 (0.81–1.28) | 0.98 |
| LRTIs | 1.15 (0.85–1.55) | 0.98 (0.70–1.30) | 1.00 (0.69–1.45) | 0.99 |
| All infections | 1.17 (1.02–1.35)* | 1.08 (0.93–1.24) | 1.00 (0.82–1.26) | 0.29 |

CI, confidence interval.

*Model included mother’s age, season of birth, year of birth, breast-feeding duration, sex, socioeconomic status of the caregiver, tobacco use during pregnancy, village of residence, and number of children living with the participant. **Incidence RR when the given quartile was compared to the first quartile of exposure (Poisson regression). *p-Values for trends were calculated by Poisson regression in which the contaminant concentration (lipid-based) was entered as a continuous variable (log-transformed). **Only infections with a mean incidence > 1.0 episode/year/infant were included; see details in “Materials and Methods.” *p < 0.05.
which medical attention was not sought by the parents. Furthermore, we did not find a suitable proxy for the propensity to go to the clinic when symptoms were present (health services are free of charge in Canada). Our results are therefore likely to be an underestimation of the true incidence. This underestimation is expected to be present for benign infection, but is unlikely to be significant for LRTIs. This underestimation may be associated with traditional lifestyle, and thus with OC exposure, but the direction of the bias is unknown. However, if such a bias was present, we could assume that it would have persisted beyond 6 months of age. RRs for the 12-month follow-up are close to unity; therefore, the bias seems to have little effect on our results.

Because of the relatively small number of subjects involved (n = 199), our results must be regarded with caution. Many factors can greatly influence the rate of acute infections. We have assessed several potential confounding factors, but unknown factors might still be present. Specifically, we cannot rule out the possibility that the infants in the lowest exposure group (first quartile) had better general health due to an unknown cause or simply due to chance. This would have resulted in RRs above the unity for the three highest quartiles of exposure without any dose–response association, which is similar to what we observed. This should be kept in mind in interpreting our results.

The high rate of infectious episodes in young Inuit children has been observed in northern Canada, the United States (Alaska), and Greenland (Banerji et al. 2001; Holman et al. 2001; Koch et al. 2002; Proulx 1988; Wainwright 1996). Many cultural, environmental, and economical factors contribute to this situation. Our study population is no exception, with a mean of almost nine infection-related medical consultations per infant during the first 12 months of life. In the context of such a high rate of infections, rate ratios of around 1.25, like the ones observed in this study, could have a tremendous impact on the public health of this population. This is the second study identifying a possible association between acute infections and prenatal exposure to OCs in Nunavik. However, the relatively small number of subjects raises the possibility of an association that could be due to chance. To further clarify the potential contribution of persisting contaminants in the high infection rate of these children, we are currently conducting another study in which a third cohort of Inuit children from the same population is being followed during the first 5 years of life. Other studies are also needed to identify which immune mechanisms are involved and to better understand the role of maternal passive immunity in these infants.

In the meantime, awareness and precautions regarding the selection of marine food items before and during pregnancies are warranted.

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