



LUND UNIVERSITY

Weight and height at 4 and 7 years of age in children born to mothers with a high intake of fish contaminated with persistent organochlorine pollutants.

Rylander, Lars; Strömberg, Ulf; Hagmar, Lars

Published in:
Chemosphere

DOI:
[10.1016/j.chemosphere.2006.09.089](https://doi.org/10.1016/j.chemosphere.2006.09.089)

2007

[Link to publication](#)

Citation for published version (APA):

Rylander, L., Strömberg, U., & Hagmar, L. (2007). Weight and height at 4 and 7 years of age in children born to mothers with a high intake of fish contaminated with persistent organochlorine pollutants. *Chemosphere*, 67(3), 498-504. <https://doi.org/10.1016/j.chemosphere.2006.09.089>

Total number of authors:
3

General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00



LUND UNIVERSITY
Faculty of Medicine

LU:*research*

Institutional Repository of Lund University

This is an author produced version of a paper published in Chemosphere. This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

Citation for the published paper:

Rylander, Lars and Stromberg, Ulf and Hagmar, Lars.
"Weight and height at 4 and 7 years of age in children
born to mothers with a high intake of fish contaminated
with persistent organochlorine pollutants"
Chemosphere, 2007, Vol: 67, Issue: 3, pp. 498-504.

<http://dx.doi.org/10.1016/j.chemosphere.2006.09.089>

Access to the published version may
require journal subscription.
Published with permission from: Elsevier

CHEM7694

Weight and height at 4 and 7 years of age in children born to mothers with a high intake of fish contaminated with persistent organochlorine pollutants

Lars Rylander¹, Ulf Strömberg¹, Lars Hagmar¹

¹Division of Occupational and Environmental Medicine and Psychiatric Epidemiology,
Department of Laboratory Medicine, University Hospital, SE-221 85 Lund, Sweden.

Correspondence and reprint requests to:

Associate professor Lars Rylander

Division of Occupational and Environmental Medicine and Psychiatric Epidemiology,
Department of Laboratory Medicine, University Hospital, SE-221 85 Lund, Sweden.

Tel: + 46 46 222 33 17; Fax: + 46 46 17 36 69; Email: lars.rylander@med.lu.se

Word count:

Abstract: 202

Text: 5597

Running title: Associations between POP and children's height and weight

Abstract

In Sweden the main exposure route for persistent organochlorine pollutants (POP) is through consumption of fatty fish from the Baltic Sea (off the eastern coast). The present study aimed to investigate whether intrauterine exposure for POP may have negative impact on children's weight and height at 4 and 7 years of age, respectively. The study included 174 fishermen's wives from the Swedish east coast who had given birth to an infant with either low (n=55) or normal (n=119) birth weight, and 88 and 206 corresponding women from the Swedish west coast (where the fish is less polluted). Comparisons between the east and west coast cohorts were performed. In addition, blood samples were collected among the east coast women and the concentrations of 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) in plasma was analyzed and estimated for the year of childbirth. There were no significant differences between the east and west coast cohorts regarding weight and height at 4 and 7 years of age. There were, however, significant negative associations between the estimated plasma concentrations of CB-153 during year of childbirth and weight at 4 and 7 years of age, respectively, among the normal birth weight children. The study gives only very weak support for the hypothesized association.

Key words: Growth, polychlorinated biphenyls, dioxin, fish

1. Background

Although human exposure to persistent organochlorine pollutants (POP) such as polychlorinated biphenyls (PCB) and dioxins has decreased during recent decades in some regions (Odsjö et al., 1997), low level exposure to these compounds are probably still important from a health perspective. In the general population in the Netherlands, in utero exposure to POP was negatively associated with birth weight and postnatal growth until 3 months of age (Patandin et al., 1998). However, no negative effects of prenatal POP exposure were found on growth rate from 3 to 42 month of age. On the other hand, such long term effects have been observed in studies from the Great Lakes in the US where negative associations between intrauterine PCB exposure through fish consumption and birth weight as well as growth until 4 years of age were seen (Fein et al., 1984; Jacobson et al., 1990). In another study, prenatal PCB exposure was negatively associated with growth among girls (Blanck et al., 2002). There are, however, also epidemiological studies showing no negative effect on growth and even a positive effect on growth after POP exposure (Rogan et al., 1987; Gladen et al., 2000; Hertz-Picciotto et al., 2005).

Negative effects of prenatal POP exposure has in animal studies been associated with reduced birth weight (Allen et al., 1980; Overman et al., 1987; Brezner et al., 1984) as well as with slower growth later on. In one study prenatal PCB exposed rats gained weight more slowly than controls during the first four month of life (Brezner et al., 1984).

In Sweden the main exposure route for POP is through consumption of fatty fish from the Baltic Sea, off the eastern coast of Sweden (Asplund et al., 1994; Svensson et al.,

1991, 1995). Fishermen's wives from the Swedish east and west coasts have reported that they consume more than twice as much fish as compared with women from the general population (Rylander et al., 1995). During the period 1973-1991 infants born to fishermen's wives from the Swedish east coast had an increased risk for lower birth weight as compared with a corresponding group from the Swedish west coast (Rylander and Hagmar, 1995), where the fish has been much less contaminated (Bergqvist et al., 1989). Case-control studies among the infants born to fishermen's wives from the Swedish east coast indicated an increased risk of lower birth weight among infants born to mothers who reported a relatively high current intake of fish from the Baltic Sea, as well as among infants born to mothers with a relatively high concentration of 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) in plasma (Rylander et al., 1996,1998). CB-153 was selected as a biomarker for POP exposure due to its very high correlations with the total PCB concentration in plasma and serum (Grimvall et al., 1997; Glynn et al., 2000), and the total POP derived 2,3,7,8-tetrachlorodibenzo-p-dioxin equivalent in plasma (Gladen et al., 1999). In addition, the PCB contribution to "dioxin-like" exposure among high consumers of fish from the Baltic Sea had been estimated to be almost 80%, whereas that from polychlorinated dioxins and furans contributed with about 20% (Asplund et al., 1994).

The aim of the present study was to investigate whether intrauterine exposure for POP may have negative impact on children's weight and height at 4 and 7 years of age, respectively.

2. Material and methods

2.1 Study base

Cohorts of fishermen's wives from the Swedish east and west coasts have previously been established (Rylander and Hagmar., 1995). These women were linked to the Swedish Medical Birth Register, which includes almost every infant born in Sweden since 1973 (Cnattingius et al., 1990). During the period 1973-1991, 757 women in the east coast cohort gave birth to 1501 children and 1834 women in the west coast cohort gave birth to 3553 children (Table 1)(Rylander et al., 1995). In the original cohort study we used 2500 g as well as 3000 g as the cut points for LBW (Rylander et al. 1995). In the following case-control study within the east coast cohort we had the intention to contrast the cases from the controls, and accordingly infants with a birth weight in the span 2750 g and 3250 g were excluded.

2.2 Selected normal and low birth weight children

In the cohorts, 89 east and 149 west coast mothers had given birth to an infant who fulfilled the following criteria: singleton, birth weight within the interval 1500-2750 g (in the present study defined as low birth weight, LBW), and without major malformation. If a mother had given birth to more than one infant with LBW, only the first infant was selected.

For each selected child with LBW two children from the cohorts were randomly selected. These children fulfilled the following criteria: singleton, birth weight within the interval 3250-4500 g (in the present study defined as normal birth weight, NBW), and without major malformation. In addition, they were matched to the LBW child according to gender, parity (1, 2, or ≥ 3), and calendar year of birth (± 5 years).

Accordingly, the results of this selection process were four groups: 1) 89 children from the east coast cohort with LBW, 2) 149 children from the west coast cohort with LBW, 3) 178 children from the east coast cohort with NBW, and 4) 298 children from the west coast cohort with NBW (Table 1). In the study one woman could only contribute with one infant.

The selected east coast children were the same as in the ones in the former case-control study that investigated the hypothesized association between POP exposure and low birth weight (Rylander et al., 1996, 1998).

2.3 Data on weight and height and potential confounders

Information about the children's weight and height in the four groups at about 4 and 7 years of age (exact ages for the measurements were always obtained) was collected in two ways. First, the mothers were contacted by telephone and asked if they could provide this information. Second, child health centers (CHS) and school health services (SHS) were contacted and asked if they could provide the requested information.

Informed consents were obtained from the mothers or the children (if they were at least 15 years of age) before such contacts were made. In Sweden, CHS are responsible for the children's health until the year when the children start the primary school (the year when the child will be 7 years of age). After that the SHS has the health responsibility.

When information was received from both sources, *i.e.* the mothers report and CHS/SHS, the data from the CHS/SHS was considered more trustworthy and was therefore primarily used in the statistical analyses. At 4 years of age, CHS data was obtained for about 75% of the participating west coast children and for slightly less than

60% of the east coast children, but there were very high correlations with data obtained from the mothers (Pearsons correlation coefficients (r) 0.95 for weight and 0.89 for height). In addition, there were no systematic differences between the two sources. At 7 years of age, SHS data were obtained for more than 90% of the children in both the east and west coast cohorts. At this age there were, however, lower correlations between the SHS data given by the mothers (0.82 for weight and 0.70 for height). In addition, the weight and height data obtained from the SHS were systematically somewhat higher, due to that the SHS measurements normally were obtained during autumn semester of the school-year, whereas the data given by the mothers were closer to the child's 7 years birthday.

At the telephone interview the women were also asked about smoking habits, education, and their own height. One person conducted all the telephone interviews. Fifty-five east coast LBW mother-child pairs participated. The corresponding figure for west coast LBW was 88, for east coast NBW 119, and for west coast NBW 206 (Table 1). Background characteristics of the participants are shown in Table 2. The study was approved by the Ethic's Committee of Lund University.

2.4 Non-participants

The age distributions were very similar among participants and non-participants. Among the east coast women the median birth year of the mothers was 1955 (range 1938, 1972) among the participating women and 1954 (1933, 1967) among the non-participants. The corresponding figures among the west coast women were 1952 (1930, 1971) and 1951 (1929, 1965), respectively. Other characteristics than birth year were unfortunately not available for the non-participants.

2.5 Exposure assessments

The cohort affiliation (east and west coast) was treated as a proxy for POP exposure. Due to the decreased levels over time of PCB in fish from the Baltic Sea (Odesjö et al., 1997), the results are also presented separately for two periods (children born 1973-1980 and 1981-1991, respectively).

For 157 (48 LBW and 109 NBW) out of the 174 (55 LBW and 119 NBW) participating east coast mothers blood samples were drawn in 1995, and the concentration of 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) in plasma was analyzed using gas chromatography with an electron capture detector (GC-ECD). The methodology for plasma extraction, clean-up, identification and quantification is given in detail elsewhere (Grimvall et al., 1997). The total lipid concentration in plasma was calculated by summation of the amounts of triglycerides, cholesterol, and phospholipids using enzymatic methods (Grimvall et al., 1997). Again, the infants had been born during the period 1973-1991, and the plasma levels of CB-153 in 1995 were probably not fully relevant for the intrauterine exposure. We did, therefore, estimate the concentrations of CB-153 in the year when the children were born with a back-calculation model where the impact of reduction of body burden at lactation, biologic half-lives during non-lactating periods, and the decrease of PCB contamination in fish over the calendar years was taken into account (Rylander et al., 1998). We made the following assumptions: 3% yearly reduction of CB-153 in the fish, 33% reduction in body burden of CB-153 at each period of lactation, and 5 years biological half-life for CB-153 during non-lactating periods. The model and a detailed discussion about the chosen assumptions has been described elsewhere (Rylander et al., 1998).

2.6 Statistics

Four outcome variables were considered: weight and height at 4 and 7 years of age, respectively. For comparisons between children with LBW from the east and west coast cohorts linear regression models were employed. We confirmed that the regression model assumption was fulfilled by residual analysis. Maternal height (three categories: ≤ 159 , 160-169, and ≥ 170 cm) and exact age (months) of the children at the time of measurement were both strongly associated with the outcome variables and were therefore always included in the multivariate models. In addition, education (9-year compulsory school, senior high school, and university), smoking habits during pregnancy (non-smokers and smokers), maternal age (≤ 24 , 25-29 and ≥ 30 years), gender and parity (1, 2, ≥ 3) were considered as potential confounders. These variables were included in the multivariate models, one at a time, and did persist in the multivariate models if they changed the point estimate with at least 15 %. In addition, to investigate possible effect modification we also performed gender specific analyses. Corresponding comparisons were performed between children with NBW from the east and west coast cohorts. Moreover, separate analyses were made within the east coast cohort for the other exposure variable, *i.e.* the mother's estimated concentration of lipid adjusted CB-153 in the year when the child was born. The CB-153 variable was analysed as a continuous variable as well as dichotomized (at the median concentration [250 ng/g lipid] and at the upper quartil 350 ng/g lipid, respectively). Due to the low number of subjects, especially for LBW (varied between 38-46 subjects), we did in the multivariate models only consider maternal height and exact age of the children at the time of measurement as potential confounders.

3. Results

Regarding weight and height at 4 and 7 years of age, respectively, there were no significant differences between children from the east and west coast cohorts (Tables 3 and 4). However, after adjustment for the confounders weight and height at 7 years of age was nearly significant lower for NBW children from the east coast born in 1973-1980, as compared with NBW children from the west coast. The results for 4 years of age were in same direction.

When the estimated plasma concentrations of CB-153 during year of childbirth among the east coast cohort women were used as exposure biomarker, no significant associations on the children's growth were observed among the LBW children. However, when concentrations of CB-153 was analyzed as a continuous variable there were, among the NBW children, significant associations with weight at 4 and 7 years, respectively. An increase of 100 ng/g lipid of CB-153 in plasma corresponded to a decrease in weight at 4 years of age of 0.4 kg (95% CI 0.01-0.7, $p=0.04$). The corresponded figure at 7 years of age was a decrease of 1.2 kg (95% CI 0.5-1.9, $p=0.001$). Similar associations were seen when concentrations of CB-153 were dichotomized. The NBW children whose mothers had CB-153 concentrations above 250 ng/g lipid had, however, significantly lower weight at 7 years of age than the NBW children whose mothers had lower concentrations of CB-153 (Table 5). The pattern was very similar when 350 ng/g lipid was used as cut-off point (data not shown).

Gender-specific analyses did not result in any obvious difference as compared to when the whole data set was analyzed (data not shown).

4. Discussion

The results from the present study did not give any strong support for the hypothesis of a negative effect of intrauterine exposure for POP on children's growth up to 4 and 7 years, respectively. However, although the associations were non-significant, it is noteworthy that seven out of the eight adjusted estimates for the comparisons between the cohorts for the early period were negative, *i.e.* showed impaired growth among the east coast children. These tendencies were more obvious among the NBW children than among the LBW children. It is important to be aware of that the outcome measurements at 4 and 7 years of age were highly correlated (r for height 0.69 and r for weight 0.74) and, accordingly, this would most probably lead to that the results for the outcome measures at 4 and 7 years of age will go in the same direction. In addition, the outcome measurements at 4 years ($r=0.74$ between height and weight) and 7 years ($r=0.69$) were also highly correlated.

Due to the relatively high proportion of non-participants in the present study, possible selection bias has to be considered. The participation rates in the two cohorts were, however, very similar, and the age distributions among participating and non-participating mothers were also very similar. Moreover, in former studies of women from the cohort of east coast fishermen's wives, where the response rate was only slightly higher, selection bias was not considered to be an issue of major concern, due to similar distributions of age, educational level and smoking habits among participants and non-participants (Rylander et al., 1996, 1998).

The information about the weight and height of the children were collected in two ways. The somewhat lower correlation between data sources at 7 years of age and the slight

systematic underestimation of the outcome measures by the mothers could be explained by that the data given by the mothers were closer to the child's 7 years birthday than the SHS data during the autumn school semester. On the other hand, this was a minor problem as SHS data was available for more than 90% of the children in both cohorts. Anyhow, this validation stresses the importance to adjust for the child's exact age in the statistical analyses.

We did, simultaneously with the children's exact age, also include the height of the mothers in the multivariate models. Unfortunately, data on the height of the fathers were only collected for the west coast cohort. The interviews with the west coast women was performed after the interviews with the east coast women and this question was the only one added. When separate analyses were performed within the west coast cohort, the height of the father was associated only with the height of the male children. At 7 years of age were, however, the height of the mothers was of greater importance than the height of the fathers. In an ongoing study, where 2436 west coast fishermen and 1082 east coast fishermen have answered a questionnaire, the median height in the two groups differed only by one cm (west coast 179 cm, east coast 178 cm, unpublished data). Accordingly, the lack of information about the fathers height in the east coast cohort did probably not confound the comparisons between the cohorts. It was not possible to link the questionnaire based data to the women in the present study.

In the present study we used cohort affiliation as a proxy measure of exposure. It is well-known that fishermen's families have a higher intake of locally caught fish as compared with individuals from the general population (Svensson et al., 1995; Rylander and Hagmar, 1995). The fatty fish from the Baltic Sea contains higher levels of POP as

291 compared with the corresponding fish from the Swedish west coast (Bergqvist et al.,
292 1989). This was clearly reflected in plasma collected from fishermen from the Swedish
293 east and west coasts, with a higher concentrations of dioxin-like POP among the east
294 coast fishermen (290 pg/g lipid) as compared with the west coast fishermen (139 pg/g
295 lipid) (Svensson et al., 1995). This taken together with the socio-economic similarities
296 between the cohorts make the cohort affiliation an appropriate proxy variable for POP
297 exposure.

298
299 We do believe that the estimated CB-153 concentrations in plasma during year of
300 childbirth is more relevant as compared with the CB-153 concentrations in 1995 (the
301 year when the samples were collected). The back-calculation model we used had
302 previously been validated (Rylander et al., 1998). In certain geographic regions in
303 Sweden, blood sera have been collected at antenatal clinics in a rubella screening
304 program. The CB-153 concentrations in 1995 and the CB-153 concentrations estimated
305 during year of rubella screening, respectively, were compared with the measured CB-
306 153 concentrations during year of rubella screening. The use of the back-calculation
307 model did clearly improve the agreement. In addition, the back-calculation model was
308 recently evaluated by Karmaus and colleagues who recommended the use of a complex
309 decay model following our strategies when repeated measurements are not available
310 (Karmaus et al., 2004). In the present study there was a very good correlation between
311 the CB-153 concentrations in 1995 and the estimated concentrations during year of
312 childbirth ($r_s=0.94$), but the concentrations during year of childbirth were generally
313 higher than in samples drawn in 1995.

314

Boys born in 1973-1975 to fishermen's wives and fishermen's sisters from the Swedish east and west coast have in a previous study been examined at 18 years of age (Rylander et al., 2000). Although the height significantly differed between the cohorts (mean height: west coast 180.1 cm and east coast 178.8 cm) the absolute difference were judged to be of little consequence. In the Lake Michigan studies, where the maternal exposure levels have been estimated to be similar to the exposure levels among fishermen's wives from the Swedish east coast (Grimvall et al., 1997), the children's growth were negatively affected until 4 years of age (Jacobson et al., 1990). There are, however, also studies which showed no negative long-term growth effects (Rogan et al., 1987; Patandin et al., 1998; Gladen et al., 2000; Hertz-Picciotto et al., 2005). Thus, including the present study, the epidemiological studies performed so far, do not give any clear evidence that dietary POP exposure may result in long term growth retardation.

329 **Acknowledgements**

330 This work was financed by grants from Swedish National Environmental Protection
331 Board, the Swedish Council for Work Life Research, and the Medical Faculty, Lund
332 University. The authors thank to Mr Sven Rylander for performing the telephone
333 interviews, Ms Anita Nilsson and Ms Margareta Kajanus for collecting the blood
334 samples, Dr Eva Grimvall for performing the analyses of CB-153, professor Peter
335 Nilsson-Ehle for performing the lipid analyses, and Ms Gunnel Nilsson for collecting
336 information from the CHS and SHS.

337

References

- Allen, J.R., Barsotti, D.A., Carstens, L.A., 1980. Residual effects of polychlorinated biphenyls on adult nonhuman primates and their offspring. *J. Toxicol. Environ. Health.* 6, 55-66.
- Asplund, L., Svensson, B.G., Nilsson, A., Eriksson, U., Jansson, B., Jensen, S., Wideqvist, U., Skerfving, S., 1994. Polychlorinated biphenyls, 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (p,p'-DDT) and 1,1-dichloro-2,2-bis(p-chlorophenyl)-ethylene (p,p'-DDE) in human plasma related to fish consumption. *Arch. Environ. Health.* 49, 477-486.
- Bergqvist, P., Bergek, S., Hallbäck, H., Rappe, C., Slorach, S., 1989. Dioxins in cod and herring from the seas around Sweden. *Chemosphere.* 19, 513-516.
- Blanck, H.M., Marcus, M., Rubin, C., Tolbert, P.E., Hertzberg, V.S., Henderson, A.K., Zhang, R.H., 2002. Growth in girls exposed in utero and postnatally to polybrominated biphenyls and polychlorinated biphenyls. *Epidemiology.* 13, 205-210.
- Brezner, E., Terekel, J., Perry, A.S., 1984. The effect of Aroclor 1254 (PCB) on the physiology of reproduction in the female rat--I. *Comp. Biochem. Physiol.* 77, 65-70.
- Cnattingius, S., Ericson, A., Gunnarskog, J., Källén, B., 1990. A quality study of a medical birth registry. *Scand. J. Soc. Med.* 18, 143-148.
- Fein, G.G., Jacobson, J.L., Jacobson, S.W., Schwartz, P.M., Dowler, J.K., 1984. Prenatal exposure to polychlorinated biphenyls: effects on birth size and gestational age. *J. Pediatr.* 105, 315-320.

- 361 Gladen, B.C., Longnecker, M.P., Schecter, A.J., 1999. Correlations among
362 polychlorinated biphenyls, dioxins, and furans in humans. *Am. J. Ind. Med.* 35,
363 15-20.
- 364 Gladen, B.C., Ragan, N.B., Rogan, W.J., 2000. Pubertal growth and development and
365 prenatal and lactational exposure to polychlorinated biphenyls and
366 dichlorodiphenyl dichloroethene. *J. Pediatr.* 136, 490-496.
- 367 Glynn, A., Wolk, A., Aune, A., Atuma, S., Zettermark, S., Maele-Schmid, M.,
368 Darnerud, P.O., Becker, W., Vessby, B., Adami, H.O., 2000. Serum
369 concentrations of organochlorines in men: a search for markers of exposure. *Sci.*
370 *Total. Environ.* 263;197-208.
- 371 Grimvall, E., Rylander, L., Nilsson-Ehle, P., Nilsson, U., Strömberg, U., Hagmar, L.,
372 Östman, C., 1997. Monitoring of polychlorinated biphenyls in human blood
373 plasma: methodological developments and influence of age, lactation, and fish
374 consumption. *Arch. Environ. Contam. Toxicol.* 32, 329-336.
- 375 Hertz-Picciotto, I., Charles, M.J., James, R.A., Keller, J.A., Willman, E., Teplin, S.,
376 2005. In utero polychlorinated biphenyls exposures in relation to fetal and early
377 childhood growth. *Epidemiology.* 16, 648-656.
- 378 Jacobson, J.L., Jacobson, S.W., Humphrey, H.E., 1990. Effects of exposure to PCBs
379 and related compounds on growth and activity in children. *Neurotoxicol.*
380 *Teratol.* 12, 319-326.
- 381 Karmaus, W., Fussman, C., Muttineni, J., Zhu, X., 2004. Backward estimation of
382 exposure to organochlorines using repeated measurements. *Env. Health.*
383 *Perspect.* 112, 710-716.
- 384 Odsjö, T., Bignert, A., Olsson, M., Asplund, L., Eriksson, U., Häggberg, L., Litzen K.,
385 de Wit, C., Rappe, C., Asplund, K., 1997. The Swedish environmental specimen

- 386 bank - Application in trend monitoring of mercury and some organohalogenated
387 compound. *Chemosphere*. 34, 2059-2066.
- 388 Overmann, S.R., Kostas, J., Wilson, L.R., Shain, W., Bush, B., 1987. Neurobehavioral
389 and somatic effects of perinatal PCB exposure in rats. *Environ. Res.* 44, 56-70.
- 390 Patandin, S., Koopman-Esseboom, C., de Ridder, M.A.J., Weisglas-Kuperus, N.,
391 Sauer, P.J.J., 1998. Effects of environmental exposure to polychlorinated
392 biphenyls and dioxins on birth size and growth in Dutch children. *Pediatr. Res.*
393 44, 538-545.
- 394 Rogan, W.J., Gladen, B.C., McKinney, J.D., Hardy, P., Thullen, J., Tingelstad, J.,
395 Tuuly, M., 1987. Polychlorinated biphenyls (PCBs) and dichlorodiphenyl
396 dichloroethene (DDE) in human milk: effects on growth, morbidity, and
397 duration of lactation. *Am. J. Public. Health*. 77, 1294-1297.
- 398 Rylander, L., Strömberg, U., Hagmar, L., 1995. Decreased birthweight among infants
399 born to women with a high dietary intake of fish contaminated with persistent
400 organochlorine compounds. *Scand. J. Work. Environ. Health*. 21, 368-375.
- 401 Rylander, L., Hagmar, L., 1995. Mortality and cancer incidence among women with a
402 high consumption of fatty fish contaminated with persistent organochlorine
403 compounds. *Scand. J. Work. Environ. Health*. 21, 419-426.
- 404 Rylander, L., Strömberg, U., Dyremark, E., Östman, C., Nilsson-Ehle, P., Hagmar, L.,
405 1998. Polychlorinated biphenyls in blood plasma among Swedish female fish
406 consumers in relation to low birth weight. *Am. J. Epidemiol.* 147, 493-502.
- 407 Rylander, L., Strömberg, U., Hagmar, L., 1996. Dietary intake of fish contaminated
408 with persistent organochlorine compounds in relation to low birthweight. *Scand.*
409 *J. Work. Environ. Health*. 22, 260-266.

- 410 Rylander, L., Hagmar, L., 2000. Medical and psychometric examinations of conscripts
411 born to mothers with a high intake of fish contaminated with persistent
412 organochlorine compounds. *Scand. J. Work. Environ. Health.* 26, 207-212.
- 413 Svensson, B.G., Nilsson, A., Hansson, M., Rappe, C., Åkesson, B., Skerfving, S., 1991.
414 Exposure to dioxins and dibenzofurans through the consumption of fish. *N. Engl.*
415 *J. Med.* 324, 8-12.
- 416 Svensson, B.G., Nilsson, A., Jonsson, E., Schütz, A., Åkesson, B., Hagmar, L., 1995.
417 Fish consumption and exposure to persistent organochlorine compounds,
418 mercury, selenium and methylamines among Swedish fishermen. *Scand. J.*
419 *Work. Environ. Health.* 21, 96-105.

Table 1. Number of children in the original cohort and in the present study.

	West coast		East coast	
	N	%	N	%
The original cohorts 1973-1991				
Number of children born	3553		1501	
Women given birth	1834		757	
Selected children for the present study				
LBW ^a	149		89	
NBW ^b	298		178	
Participants in the present study ^c				
LBW ^a	88	59	55	62
NBW ^b	206	69	119	67

^a Children with a birth weight between 1500 and 2750 g, defined as low birth weight (LBW).

^b Children with a birth weight between 3250 and 4500 g, defined as normal birth weight (NBW).

^c Children with information of height or weight at 4 or 7 years of age.

428 **Table 2.** Background and exposure characteristics of the maternal and child participants in the present study.
 429

	West coast				East coast			
	LBW (n=88) ^a		NBW (n=206) ^b		LBW (n=55) ^a		NBW (n=119) ^b	
	%	Median (5, 95 perc)	%	Median (5, 95 perc)	%	Median (5, 95 perc)	%	Median (5, 95 perc)
Maternal								
Age (yr) ^c								
≤ 24	23		28		40		21	
25-29	43		41		24		45	
≥ 30	34		32		36		34	
First parity	52		53		51		45	
Education								
Compulsory school	43		32		33		38	
Senior high school	41		46		45		45	
University	16		22		22		16	
Smoking ^c	53		33		58		50	
Height (cm)		165 (154, 174)		167 (158, 175)		165 (158, 175)		165 (158, 175)
CB-153 (ng/g lipid) ^e								
In 1995		-		-		178 (59, 464)		159 (69, 500)
Estimated for year of childbirth ^f		-		-		295 (102, 599)		243 (97, 719)
Child								
Calendar year of birth								
1973-1980	59		56		45		44	
1981-1991	41		44		55		56	
Male gender	39		42		53		43	

Birth weight (kg)	2.43 (1.55, 2.70)	3.73 (3.29, 4.34)	2.44 (1.74, 2.73)	3.65 (3.30, 4.36)
Exact age at the 4 year examination (months)	48.2 (47.7, 53.0)	48.1 (47.6, 53.1)	48.8 (46.4, 55.1)	48.2 (46.6, 55.3)
Exact age at the 7 year examination (months)	86.7 (73.2, 91.4)	85.7 (73.9, 93.0)	87.2 (80.0, 92.2)	87.1 (78.2, 92.4)

430 ^a Children with a birth weight between 1500 and 2750 g, defined as low birth weight (LBW).

431 ^b Children with a birth weight between 3250 and 4500 g, defined as normal birth weight (NBW).

432 ^c At year of childbirth.

433 ^d Lactation for the index pregnancy.

434 ^e CB-153 is 2,2',4,4',5,5'-hexachlorobiphenyl.

435 ^f See Materials and Metho

Table 3. The effect of cohort affiliation (east versus west coast) on weight (at 4 and 7 years of age, respectively) among children with a birth weight between 1500 and 2750 g (defined as LBW). Corresponding effect among children with a birth weight between 3250 and 4500 g (defined as NBW). Unadjusted, as well as adjusted estimates with 95% confidence intervals (CI) obtained from linear regression models are shown. Moreover, the results are divided in two calendar year periods.

	Weight at 4 years of age (kg)				Weight at 7 years of age (kg)			
	Unadjusted		Adjusted ^b		Unadjusted		Adjusted ^b	
	β^a	95% CI	β^a	95% CI	β^a	95% CI	β^a	95% CI
<i>LBW</i>								
born 1973-1991	0.41	-0.34, 1.16	0.17	-0.56, 0.90	1.07	-0.59, 2.73	0.06	-1.54, 1.66
- Born 1973-1980	-0.13	-1.11, 0.84	-0.12	-1.07, 0.84	1.05	-1.10, 3.21	0.13	-1.86, 2.12
- Born 1981-1991	0.62	-0.53, 1.76	0.20	-0.99, 1.39	0.76	-1.90, 3.41	-0.14	-2.83, 2.54
<i>NBW</i>								
born 1973-1991	-0.27	-0.84, 0.31	-0.27	-0.84, 0.31	0.13	-0.83, 1.10	0.17	-0.79, 1.13
- Born 1973-1980	-0.50	-1.47, 0.46	-0.62	-1.60, 0.36	-1.21	-2.49, 0.07	-1.28	-2.58, 0.01
- Born 1981-1991	-0.12	-0.86, 0.62	-0.06	-0.80, 0.69	1.06	-0.37, 2.50	1.18	-0.22, 2.58

^a Mean differences between east and west coast cohort children.

^b Adjusted for the children's exact age (in month) and height of the mother (<160, 160-169, and ≥ 170 cm).

Table 4. The effect of cohort affiliation (east versus west coast) on height (at 4 and 7 years of age, respectively) among children with a birth weight between 1500 and 2750 g (defined as LBW), and corresponding effect among children with a birth weight between 3250 and 4500 g (defined as NBW). Unadjusted, as well as adjusted estimates with 95% confidence intervals (CI) obtained from linear regression models are shown. Moreover, the results are divided in two calendar year periods.

	Height at 4 years of age (cm)				Height at 7 years of age (cm)			
	Unadjusted		Adjusted ^b		Unadjusted		Adjusted ^b	
	β^a	95% CI	β^a	95% CI	β^a	95% CI	β^a	95% CI
<i>LBW</i>								
born 1973-1991	0.84	-0.74, 2.41	0.09	-1.43, 1.61	2.22	-0.19, 4.63	0.26	-1.80, 2.31
- Born 1973-1980	-0.32	-2.64, 2.00	-0.50	-2.73, 1.74	0.73	-2.64, 4.10	-1.33	-3.61, 0.96
- Born 1981-1991	1.30	-0.93, 3.53	-0.03	-2.32, 2.26	2.73	-0.75, 6.20	1.51	-1.98, 4.99
<i>NBW</i>								
born 1973-1991	-0.40	-1.46, 0.66	-0.55	-1.53, 0.43	-0.10	-1.33, 1.12	-0.33	-1.42, 0.76
- Born 1973-1980	-0.66	-2.49, 1.16	-1.46	-3.13, 0.22	-1.01	-2.76, 0.73	-1.46	-3.06, 0.13
- Born 1981-1991	-0.13	-1.49, 1.22	0.09	-1.17, 1.35	0.72	-1.05, 2.49	0.64	-0.88, 2.17

^a Mean differences between east and west coast cohort children.

^b Adjusted for the children's exact age (in month) and height of the mother (<160, 160-169, and ≥ 170 cm).

Table 5. The effect of maternal concentration of lipid-adjusted CB-153 (2,2',4,4',5,5'-hexachlorobiphenyl) in plasma in the year when the child was born on growth (height and weight at 4 and 7 years of age, respectively) among children born to fishermen's wives from the Swedish east coast. Estimates with 95% confidence intervals (CI) obtained from linear regression models are shown. Moreover, the results are divided in children with low birth weight (LBW) and children with normal birth weight (NBW).

	Growth at 4 years of age				Growth at 7 years of age			
	Weight (kg)		Height (cm)		Weight (kg)		Height (cm)	
	β^a	95% CI	β^a	95% CI	β^a	95% CI	β^a	95% CI
<i>LBW</i>								
Crude ^b	-1.34	-2.74, 0.05	-1.16	-4.08, 1.77	0.26	-2.50, 3.02	-2.50	-6.97, 1.96
Adjusted ^c	-1.05	-2.51, 0.42	-0.21	-2.91, 2.49	0.73	-1.93, 3.39	-1.69	-6.06, 2.69
<i>NBW</i>								
Crude ^b	-0.12	-1.02, 0.79	0.92	-0.75, 2.60	-1.67	-3.37, 0.02	0.14	-1.78, 2.06
Adjusted ^c	-0.39	-1.21, 0.44	0.35	-1.08, 1.79	-2.00	-3.63, -0.37	-0.31	-2.05, 1.43

^a Mean differences between children whose mothers had plasma concentrations of CB-153 greater than 250 ng/g lipid compared with those whose mothers had lower concentrations.

^b Univariate models

^c Adjusted for the children's exact age (in month) and height of the mother (<160, 160-169, and \geq 170 cm).