Table S1. Distributions of dioxin-like congeners in maternal blood (pg/g lipids).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Dioxin-like congener | Detection  | Detection  | Toxic equivalency factor | Male (n = 85) | 　 | Female (n = 98) |
| limit (pg/g lipid) | rate (%) | Median (IQR) | 　 | Median (IQR) |
| 2,3,7,8-TCDD | 1 | 46.8 | 1 | ND (ND, 1.28) |  | ND (ND, 1.30) |
| 1,2,3,7,8-Penta-CDD | 1 | 98.1 | 1 | 4.09 (3.16, 5.24) |  | 3.92 (2.63, 4.81) |
| 1,2,3,4,7,8-Hexa-CDD | 2 | 41.1 | 0.1 | ND (ND, 2.54) |  | ND (ND, 2.19) |
| 1,2,3,6,7,8-Hexa-CDD | 2 | 100 | 0.1 | 14.4 (9.78, 18.6) |  | 13.0 (9.86, 16.7) |
| 1,2,3,7,8,9-Hexa-CDD | 2 | 55.9 | 0.1 | 2.25 (ND, 3.07) |  | 2.21 (ND, 3.02) |
| 1,2,3,4,6,7,8-Hepta-CDD | 2 | 100 | 0.01 | 23.7 (19.8, 33.2) |  | 24.6 (20.3, 30.8) |
| OCDD | 4 | 100 | 0.0003 | 432 (352, 583) |  | 411 (352, 579) |
| 2,3,7,8-TCDF | 1 | 23.6 | 0.1 | ND (ND, 1.12) |  | ND (ND, 0.63) |
| 1,2,3,7,8-Penta-CDF | 1 | 8.4 | 0.03 | ND (ND, ND) |  | ND (ND, ND) |
| 2,3,4,7,8-Penta-CDF | 1 | 99.6 | 0.3 | 5.90 (4.34, 7.30) |  | 5.66 (4.11, 6.84) |
| 1,2,3,4,7,8-Hexa-CDF | 2 | 62 | 0.1 | 2.41 (ND, 3.29) |  | 2.41 (ND, 2.91) |
| 1,2,3,6,7,8-Hexa-CDF | 2 | 71.5 | 0.1 | 2.69 (2.17, 4.07) |  | 2.54 (ND, 3.52) |
| 2,3,4,6,7,8-Hexa-CDF | 2 | 4.2 | 0.1 | ND (ND, ND) |  | ND (ND, ND) |
| 1,2,3,7,8,9-Hexa-CDF | 2 | 0 | 0.1 | ND (ND, ND) |  | ND (ND, ND) |
| 1,2,3,4,6,7,8-Hepta-CDF | 2 | 65 | 0.01 | 2.61 (ND, 3.47) |  | 2.30 (ND, 3.11) |
| 1,2,3,4,7,8,9-Hepta-CDF | 2 | 0.4 | 0.01 | ND |  | ND |
| OCDF | 4 | 1.1 | 0.0003 | ND |  | ND |
| 344'5-TCB (#81) | 10 | 0 | 0.0003 | ND |  | ND |
| 33'44'-TCB (#PCB 77) | 10 | 68.8 | 0.0001 | 12.0 (10.1, 15.0) |  | 11.7 (ND, 14.7) |
| 33'44'5-Penta-CB (#126) | 10 | 97 | 0.1 | 35.8 (25.1, 47.2) |  | 32.3 (20.7, 53.8) |
| 33'44'55'-Hexa-CB (#169) | 10 | 94.7 | 0.03 | 25.4 (18.9, 32.1) |  | 23.3 (15.5, 31.2) |
| 2’344’5-Penta-CB (#123) | 10 | 99.6 | 0.00003 | 119 (87.0, 161) |  | 104 (69.6, 165) |
| 23'44'5-Penta-CB (#118) | 10 | 100 | 0.00003 | 6396 (4196, 8334) |  | 5665 (4090, 9296) |
| 2344'5-Penta-CB (#114) | 10 | 99.6 | 0.00003 | 357 (276, 490) |  | 366 (226, 503) |
| 233'44'-Penta-CB (#105) | 10 | 100 | 0.00003 | 1505 (1061, 2182) |  | 1382 (1000, 2263) |
| 23'44'55'-Hexa-CB (#167) | 10 | 100 | 0.00003 | 778 (514, 1005) |  | 711 (484, 986) |
| 233'44'5-Hexa-CB (#156) | 10 | 100 | 0.00003 | 2045 (1408, 2918) |  | 1915 (1312, 2590) |
| 233'44'5'-Hexa-CB (#157) | 10 | 100 | 0.00003 | 484 (344, 702) |  | 468 (353, 655) |
| 233'44'55'-Hepta-CB (#189) | 10 | 100 | 0.00003 | 235 (174, 335) | 　 | 237 (171, 334) |

Table S2. Maternal and infant characteristics in relation to maternal dioxin-like compounds (DLCs) and cord hormones (n = 183).

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | 　 | Total DLCs | 　 | Progesterone (ng/mL) | 　 | E2 (ng/mL) | 　 | T (pg/mL) |
| 　 | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) |
| Maternal characteristics  |  |  |  |  |  |  |  |  |  |  |  |  |
|  Age at delivery (years) |  | 0.234\*\* |  |  | -0.140 |  |  | -0.199\*\* |  |  | 0.024 |  |
|  Pre-pregnancy BMI (m2/kg) |  | 0.085 |  |  | -0.042 |  |  | -0.109 |  |  | -0.048 |  |
|  Blood sampling weeks during pregnancy |  | -0.057 |  |  |  |  |  |  |  |  |  |  |
|  Parity |  |  |  |  |  |  |  |  |  |  |  |  |
| 0 |  |  | 15.2 (12.6, 19.6)\*\* |  |  | 240 (188, 305)\* |  |  | 5.41 (3.97, 7.73)\*\* |  |  | 80.3 (58.9, 113) |
| ≥1 |  |  | 13.3 (9.0, 17.8) |  |  | 209 (174, 265) |  |  | 4.38 (3.15, 6.73) |  |  | 89.4 (64.5, 118) |
|  Education level (years) |  |  |  |  |  |  |  |  |  |  |  |  |
| ≤12 |  |  | 13.9 (9.8, 18.0) |  |  | 229 (173, 295) |  |  | 5.10 (3.29, 7.03) |  |  | 84.8 (59.6, 116) |
| ≥12 |  |  | 15.0 (11.5, 19.6) |  |  | 223 (183, 266) |  |  | 5.02 (3.61, 7.51) |  |  | 83.7 (59.9, 114) |
|  Tobacco smoking during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
| Nonsmoker |  |  | 14.8 (11.2, 19.1) |  |  | 219 (175, 278) |  |  | 4.86 (3.44, 7.07) |  |  | 84.6 (60.1, 116) |
| Smoker |  |  | 12.2 (8.9, 17.3) |  |  | 240 (187, 267) |  |  | 5.91 (4.10, 7.59) |  |  | 83.0 (58.2, 114) |
|  Alcohol consumption during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
| No |  |  | 14.6 (9.5, 18.1) |  |  | 228 (184, 275) |  |  | 5.12 (3.64, 7.30) |  |  | 81.1 (59.0, 112) |
| Yes |  |  | 14.4 (11.7, 18.7) |  |  | 212 (175, 282) |  |  | 4.76 (3.36, 7.19) |  |  | 93.0 (61.9, 123) |
|  Annual household income (million yen) |  |  |  |  |  |  |  |  |  |  |  |  |
| <5 |  |  | 13.8 (9.9, 17.7)\* |  |  | 225 (184, 278) |  |  | 5.02 (3.57, 7.18) |  |  | 85.7 (58.9, 115) |
| ≥5 |  |  | 15.8 (12.1, 20.8) |  |  | 223 (161, 275) |  |  | 5.23 (3.48, 7.59) |  |  | 82.4 (62.8, 131) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infant characteristics |  |  |  |  |  |  |  |  |  |  |  |  |
|  Gestational age at birth (weeks) |  | 0.060 |  |  | -0.089 |  |  | -0.065 |  |  | -0.158\* |  |
|  Birth weight (g) |  |  |  |  |  |  |  |  |  |  |  |  |
| Male |  | -0.039 |  |  | 0.176 |  |  | 0.066 |  |  | -0.004 |  |
| Female | 　 | -0.006 | 　 | 　 | -0.006 | 　 | 　 | -0.168 | 　 | 　 | -0.094 | 　 |

E2, estradiol; T, testosterone; IQR, interquartile range.

\*p < 0.05, \*\*p < 0.01 were calculated using the Spearman rank test or the Mann–Whitney U test.

Table S2. (continued)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | 　 | T/E2 | 　 | Androstenedione (ng/mL) | 　 | DHEA (ng/mL) | 　 | Cortisol (ng/mL) |
| 　 | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) |
| Maternal characteristics  |  |  |  |  |  |  |  |  |  |  |  |  |
|  Age at delivery (years) |  | 0.261\*\* |  |  | -0.051 |  |  | -0.071 |  |  | -0.200\*\* |  |
|  Pre-pregnancy BMI (m2/kg) |  | 0.053 |  |  | 0.022 |  |  | 0.043 |  |  | 0.058 |  |
|  Blood sampling weeks during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
|  Parity |  |  |  |  |  |  |  |  |  |  |  |  |
| 0 |  |  | 14.6 (10.8, 19.6) |  |  | 0.44 (0.35, 0.57) |  |  | 2.37 (1.84, 3.29) |  |  | 56.5 (34.0, 84.6)\*\* |
| ≥1 |  |  | 18.7 (14.5, 26.0) |  |  | 0.47 (0.39, 0.58) |  |  | 2.16 (1.77, 2.96) |  |  | 27.7 (19.6, 48.8) |
|  Education level (years) |  |  |  |  |  |  |  |  |  |  |  |  |
| ≤12 |  |  | 17.6 (12.9, 24.4) |  |  | 0.47 (0.39, 0.62) |  |  | 2.31 (1.90, 2.93) |  |  | 41.1 (22.4, 68.4) |
| ≥12 |  |  | 16.4 (12.0, 21.9) |  |  | 0.45 (0.35, 0.57) |  |  | 2.26 (1.71, 3.21) |  |  | 41.7 (23.5, 66.8) |
|  Tobacco smoking during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
| Nonsmoker |  |  | 17.4 (12.8, 23.2)\* |  |  | 0.45 (0.36, 0.57) |  |  | 2.22 (1.76, 2.97) |  |  | 41.0 (22.2, 66.9) |
| Smoker |  |  | 14.1 (11.1, 18.6) |  |  | 0.51 (0.40, 0.64) |  |  | 2.67 (2.00, 3.74) |  |  | 49.3 (27.3, 79.5) |
|  Alcohol consumption during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
| No |  |  | 16.2 (12.4, 22.1) |  |  | 0.45 (0.36, 0.57) |  |  | 2.22 (1.71, 2.97) |  |  | 48.3 (24.8, 75.3)\* |
| Yes |  |  | 17.7 (12.6, 23.1) |  |  | 0.47 (0.38, 0.61) |  |  | 2.34 (1.98, 3.31) |  |  | 37.1 (20.6, 52.3) |
|  Annual household income (million yen) |  |  |  |  |  |  |  |  |  |  |  |  |
| <5 |  |  | 16.3 (12.4, 22.1)\* |  |  | 0.47 (0.36, 0.60) |  |  | 2.25 (1.77, 2.98) |  |  | 41.2 (25.3, 67.8) |
| ≥5 |  |  | 17.0 (12.6, 22.8) |  |  | 0.43 (0.35, 0.53) |  |  | 2.32 (1.81, 3.42) |  |  | 41.2 (20.7, 60.0) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infant characteristics |  |  |  |  |  |  |  |  |  |  |  |  |
|  Gestational age at birth (weeks) |  | -0.068 |  |  | -0.043 |  |  | 0.023 |  |  | 0.174\* |  |
|  Birth weight (g) |  |  |  |  |  |  |  |  |  |  |  |  |
| Male |  | -0.112 |  |  | 0.159 |  |  | -0.060 |  |  | 0.100 |  |
| Female | 　 | 0.002 | 　 | 　 | -0.112 | 　 | 　 | -0.105 | 　 | 　 | 0.005 | 　 |

E2, estradiol; T, testosterone; IQR, interquartile range, DHEA, dehydroepiandrosterone.

\*p < 0.05, \*\*p < 0.01 were calculated using the Spearman rank test or the Mann–Whitney U test.

Table S2. (continued)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | 　 | Cortisone (ng/mL) | 　 | Adrenal androgen/glucocorticoid ratioc | 　 | SHBG (nmol/L) | 　 | Prolactin (ng/mL) |
| 　 | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) |
| Maternal characteristics  |  |  |  |  |  |  |  |  |  |  |  |  |
|  Age at delivery (years) |  | -0.202\*\* |  |  | 0.125 |  |  | -0.029 |  |  | -0.019 |  |
|  Pre-pregnancy BMI (m2/kg) |  | 0.047 |  |  | -0.015 |  |  | -0.113 |  |  | -0.068 |  |
|  Blood sampling weeks during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
|  Parity |  |  |  |  |  |  |  |  |  |  |  |  |
| 0 |  |  | 114.8 (85.0, 135)\*\* |  |  | 0.02 (0.01, 0.03)\*\* |  |  | 16.2 (14.4, 18.9)\* |  |  | 89.1 (58.6, 122) |
| ≥1 |  |  | 82.4 (65.5, 104) |  |  | 0.02 (0.02, 0.04) |  |  | 15.0 (12.8, 18.1) |  |  | 80.8 (64.3, 113) |
|  Education level (years) |  |  |  |  |  |  |  |  |  |  |  |  |
| ≤12 |  |  | 97.4 (68.7, 123) |  |  | 0.02 (0.01, 0.03) |  |  | 15.5 (13.6, 18.4) |  |  | 85.5 (61.5, 131) |
| ≥12 |  |  | 96.7 (73.6, 126) |  |  | 0.02 (0.01, 0.03) |  |  | 15.7 (13.5, 18.7) |  |  | 88.6 (67.1, 115) |
|  Tobacco smoking during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
| Nonsmoker |  |  | 95.3 (67.9, 128) |  |  | 0.02 (0.01, 0.03) |  |  | 15.2 (12.9, 17.5)\*\* |  |  | 82.8 (59.4, 116) |
| Smoker |  |  | 98.0 (82.9, 117) |  |  | 0.02 (0.01, 0.03) |  |  | 18.3 (15.5, 20.2) |  |  | 99.9 (66.1, 130) |
|  Alcohol consumption during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
| No |  |  | 97.2 (77.4, 128) |  |  | 0.02 (0.01, 0.03)\*\* |  |  | 15.8 (13.6, 18.5) |  |  | 88.9 (62.0, 125) |
| Yes |  |  | 93.8 (63.3, 118) |  |  | 0.02 (0.02, 0.04) |  |  | 15.3 (13.5, 18.8) |  |  | 82.9 (62.4, 105) |
|  Annual household income (million yen) |  |  |  |  |  |  |  |  |  |  |  |  |
| <5 |  |  | 97.0 (74.9, 127) |  |  | 0.02 (0.01, 0.03) |  |  | 15.4 (13.2, 18.9) |  |  | 87.4 (59.7, 116) |
| ≥5 |  |  | 93.9 (65.5, 124) |  |  | 0.02 (0.01, 0.03) |  |  | 15.9 (14.2, 18.5) |  |  | 80.8 (67.0, 125) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infant characteristics |  |  |  |  |  |  |  |  |  |  |  |  |
|  Gestational age at birth (weeks) |  | 0.083 |  |  | -0.093 |  |  | 0.265\*\* |  |  | 0.109 |  |
|  Birth weight (g) |  |  |  |  |  |  |  |  |  |  |  |  |
| Male |  | 0.258\* |  |  | -0.144 |  |  | 0.095 |  |  | -0.038 |  |
| Female | 　 | -0.028 | 　 | 　 | -0.035 | 　 | 　 | -0.048 | 　 | 　 | 0.066 | 　 |

SHBG, sex hormone-binding globulin; IQR, interquartile range.

Adrenal androgen/glucocorticoid ratio = (DHEA and androstenedione)/(cortisol and cortisone)

\*p < 0.05, \*\*p < 0.01 were calculated using the Spearman rank test or the Mann–Whitney U test.

Table S2. (continued)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | 　 | LH (mIU/mL) | 　 | FSH (mIU/mL) | 　 | Inhibin B (pg/mL) | 　 | INSL3 (ng/mL) |
| 　 | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) | 　 | r |  Median (IQR) |
| Maternal characteristics  |  |  |  |  |  |  |  |  |  |  |  |  |
|  Age at delivery (years) |  | 0.227\* |  |  | 0.244\* |  |  | 0.069 |  |  | -0.033 |  |
|  Pre-pregnancy BMI (m2/kg) |  | 0.016 |  |  | 0.070 |  |  | -0.177 |  |  | -0.162 |  |
|  Blood sampling weeks during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
|  Parity |  |  |  |  |  |  |  |  |  |  |  |  |
| 0 |  |  | 0.25 (0.25, 1.06) |  |  | 0.25 (0.25, 0.65) |  |  | 43.8 (35.8, 57.9) |  |  | 0.29 (0.23, 0.32) |
| ≥1 |  |  | 0.25 (0.25, 0.68) |  |  | 0.39 (0.25, 0.69) |  |  | 43.0 (30.9, 58.6) |  |  | 0.28 (0.25, 0.31) |
|  Education level (years) |  |  |  |  |  |  |  |  |  |  |  |  |
| ≤12 |  |  | 0.25 (0.25, 0.85) |  |  | 0.25 (0.25, 0.65) |  |  | 48.2 (32.1, 60.0) |  |  | 0.29 (0.26, 0.32) |
| ≥12 |  |  | 0.25 (0.25, 0.93) |  |  | 0.25 (0.25, 0.71) |  |  | 42.8 (34.2, 57.8) |  |  | 0.28 (0.24, 0.32) |
|  Tobacco smoking during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
| Nonsmoker |  |  | 0.25 (0.25, 0.93) |  |  | 0.25 (0.25, 0.70) |  |  | 43.6 (33.6, 58.5) |  |  | 0.28 (0.26, 0.32) |
| Smoker |  |  | 0.25 (0.25, 0.25) |  |  | 0.25 (0.25, 0.61) |  |  | 40.6 (32.6, 60.1) |  |  | 0.27 (0.23, 0.30) |
|  Alcohol consumption during pregnancy |  |  |  |  |  |  |  |  |  |  |  |  |
| No |  |  | 0.25 (0.25, 1.12) |  |  | 0.25 (0.25, 0.71) |  |  | 42.8 (32.2, 57.6) |  |  | 0.28 (0.24, 0.31) |
| Yes |  |  | 0.25 (0.25, 0.81) |  |  | 0.25 (0.25, 0.64) |  |  | 44.4 (35.0, 60.6) |  |  | 0.29 (0.26, 0.35) |
|  Annual household income (million yen) |  |  |  |  |  |  |  |  |  |  |  |  |
| <5 |  |  | 0.25 (0.25, 0.89) |  |  | 0.25 (0.25, 0.65) |  |  | 43.0 (34.5, 60.9) |  |  | 0.29 (0.24, 0.32) |
| ≥5 |  |  | 0.25 (0.25, 0.87) |  |  | 0.56 (0.25, 0.74) |  |  | 46.4 (30.6, 58.3) |  |  | 0.27 (0.25, 0.34) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infant characteristics |  |  |  |  |  |  |  |  |  |  |  |  |
|  Gestational age at birth (weeks) |  | -0.095 |  |  | -0.071 |  |  | 0.256\* |  |  | -0.216 |  |
|  Birth weight (g) |  |  |  |  |  |  |  |  |  |  |  |  |
| Male |  | -0.187 |  |  | -0.027 |  |  | 0.031 |  |  | 0.038 |  |
| Female | 　 | 　 | 　 | 　 | 　 | 　 | 　 | 　 | 　 | 　 | 　 | 　 |

FSH, follicle stimulating hormone; INSL3, insulin-like factor 3; LH, luteinizing hormone; IQR, interquartile range.

\*p < 0.05, \*\*p < 0.01 were calculated using the Spearman rank test or the Mann–Whitney U test.

Table S3. Adjusted linear regression coefficients (B) and 95% confidence intervals (CI) for reproductive and steroid hormone levels in cord blood in relation to dioxin-like congeners in maternal blood stratified by sex (pg/g lipids).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 　 | 　 | 　 | T/E2 | 　 | DHEA | 　 | Cortisol | 　 | Cortisone | 　 | Adrenal androgen/glucocorticoid ratioa | 　 | SHBG |
| 　 | 　 | 　 | B (95% CI) | 　 | B (95% CI) | 　 | B (95% CI) | 　 | B (95% CI) | 　 | B (95% CI) | 　 | B (95% CI) |
| Male | PCDDs | 1,2,3,7,8-Penta-CDD | -0.08 (-0.38, 0.23) |  | 0.39 (0.02, 0.75)\* |  | -0.36 (-1.13, 0.40) |  | -0.53 (-1.51, 0.46) |  | 0.77 (-0.34, 1.89) |  | -0.08 (-0.22, 0.06) |
|  |  | 1,2,3,6,7,8-Hexa-CDD | -0.29 (-0.60, 0.01) |  | 0.38 (0.01, 0.75)\* |  | -0.37 (-1.15, 0.40) |  | -0.56 (-1.56, 0.44) |  | 0.81 (-0.31, 1.94) |  | -0.10 (-0.25, 0.04) |
|  |  | 1,2,3,4,6,7,8-Hepta-CDD | -0.23 (-0.55, 0.10) |  | 0.25 (-0.15, 0.66) |  | 0.06 (-0.77, 0.89) |  | -0.28 (-1.35, 0.79) |  | 0.37 (-0.84, 1.58) |  | -0.13 (-0.28, 0.02) |
|  |  | OCDD | -0.22 (-0.53, 0.09) |  | 0.25 (-0.14, 0.63) |  | -0.01 (-0.80, 0.78) |  | -0.29 (-1.31, 0.73) |  | 0.42 (-0.73, 1.57) |  | -0.08 (-0.22, 0.07) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | PCDFs | 2,3,4,7,8-Penta-CDF | -0.24 (-0.58, 0.10) |  | 0.36 (-0.05, 0.77) |  | -0.72 (-1.56, 0.11) |  | -0.88 (-1.96, 0.21) |  | 1.08 (-0.14, 2.31) |  | -0.11 (-0.27, 0.05) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Non-ortho PCBs | 33'44'5-Penta-CB (#126) | -0.21 (-0.38, -0.03)\* |  | 0.29 (0.07, 0.51)\*\* |  | -0.40 (-0.85, 0.05) |  | -0.53 (-1.12, 0.05) |  | 0.71 (0.05, 1.37)\* |  | -0.10 (-0.18, -0.02)\* |
|  |  | 33'44'55'-Hexa-CB (#169) | -0.20 (-0.46, 0.06) |  | 0.29 (-0.03, 0.60) |  | -0.67 (-1.30, -0.03)\* |  | -0.70 (-1.53, 0.13) |  | 0.90 (-0.04, 1.84) |  | -0.10 (-0.22, 0.02) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Mono-ortho PCBs | 2’344’5-Penta-CB (#123) | -0.18 (-0.39, 0.02) |  | 0.26 (0.01, 0.50)\* |  | -0.21 (-0.72, 0.30) |  | -0.21 (-0.72, 0.30) |  | 0.51 (-0.23, 1.26) |  | -0.07 (-0.17, 0.02) |
|  |  | 23'44'5-Penta-CB (#118) | -0.22 (-0.45, 0.01) |  | 0.27 (-0.02, 0.55) |  | -0.32 (-0.91, 0.27) |  | -0.49 (-1.24, 0.27) |  | 0.64 (-0.22, 1.49) |  | -0.09 (-0.20, 0.02) |
|  |  | 2344'5-Penta-CB (#114) | -0.20 (-0.47, 0.06) |  | 0.22 (-0.11, 0.54) |  | -0.32 (-0.98, 0.35) |  | -0.31 (-1.18, 0.55) |  | 0.50 (-0.47, 1.48) |  | -0.06 (-0.18, 0.07) |
|  |  | 233'44'-Penta-CB (#105) | -0.23 (-0.44, -0.02)\* |  | 0.27 (0.01, 0.52)\* |  | -0.33 (-0.87, 0.20) |  | -0.51 (-1.20, 0.18) |  | 0.66 (-0.12, 1.43) |  | -0.09 (-0.19, 0.01) |
|  |  | 23'44'55'-Hexa-CB (#167) | -0.16 (-0.43, 0.11) |  | 0.24 (-0.09, 0.57) |  | -0.34 (-1.02, 0.34) |  | -0.48 (-1.36, 0.39) |  | 0.62 (-0.37, 1.61) |  | -0.06 (-0.19, 0.07) |
|  |  | 233'44'5-Hexa-CB (#156) | -0.11 (-0.42, 0.21) |  | 0.14 (-0.24, 0.53) |  | -0.37 (-1.15, 0.42) |  | -0.24 (-1.26, 0.78) |  | 0.41 (-0.75, 1.57) |  | -0.07 (-0.22, 0.08) |
|  |  | 233'44'5'-Hexa-CB (#157) | -0.13 (-0.40, 0.14) |  | 0.20 (-0.13, 0.53) |  | -0.28 (-0.95, 0.39) |  | -0.29 (-1.17, 0.58) |  | 0.47 (-0.52, 1.45) |  | -0.05 (-0.18, 0.07) |
|  |  | 233'44'55'-Hepta-CB (#189) | 0.00 (-0.28, 0.28) |  | 0.00 (-0.34, 0.34) |  | -0.20 (-0.89, 0.49) |  | -0.08 (-0.98, 0.82) |  | 0.11 (-0.91, 1.13) |  | -0.05 (-0.17, 0.08) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Female | PCDDs | 1,2,3,7,8-Penta-CDD | 0.17 (-0.12, 0.45) |  | 0.03 (-0.34, 0.39) |  | 0.17 (-0.51, 0.85) |  | 0.25 (-0.66, 1.16) |  | -0.16 (-1.21, 0.90) |  | 0.14 (-0.13, 0.41) |
|  |  | 1,2,3,6,7,8-Hexa-CDD | 0.07 (-0.23, 0.37) |  | 0.23 (-0.15, 0.61) |  | -0.30 (-1.02, 0.42) |  | -0.55 (-1.52, 0.42) |  | 0.63 (-0.48, 1.75) |  | 0.07 (-0.22, 0.36) |
|  |  | 1,2,3,4,6,7,8-Hepta-CDD | 0.13 (-0.23, 0.49) |  | -0.20 (-0.66, 0.25) |  | 0.66 (-0.19, 1.51) |  | 0.75 (-0.40, 1.89) |  | -0.88 (-2.20, 0.44) |  | 0.32 (-0.02, 0.66) |
|  |  | OCDD | 0.13 (-0.22, 0.49) |  | -0.04 (-0.50, 0.42) |  | 0.48 (-0.37, 1.34) |  | 0.63 (-0.52, 1.77) |  | -0.59 (-1.92, 0.73) |  | 0.29 (-0.05, 0.63) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | PCDFs | 2,3,4,7,8-Penta-CDF | 0.11 (-0.16, 0.39) |  | 0.16 (-0.18, 0.51) |  | -0.03 (-0.69, 0.62) |  | -0.06 (-0.93, 0.82) |  | 0.23 (-0.78, 1.24) |  | 0.14 (-0.12, 0.40) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Non-ortho PCBs | 33'44'5-Penta-CB (#126) | 0.18 (-0.05, 0.40) |  | -0.17 (-0.45, 0.12) |  | 0.20 (-0.34, 0.75) |  | 0.36 (-0.37, 1.08) |  | -0.41 (-1.24, 0.43) |  | 0.17 (-0.05, 0.38) |
|  |  | 33'44'55'-Hexa-CB (#169) | 0.00 (-0.26, 0.26) |  | 0.18 (-0.15, 0.51) |  | -0.13 (-0.75, 0.49) |  | -0.07 (-0.90, 0.76) |  | 0.28 (-0.68, 1.24) |  | 0.15 (-0.10, 0.40) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Mono-ortho PCBs | 2’344’5-Penta-CB (#123) | 0.24 (0.00, 0.47)\* |  | -0.29 (-0.58, 0.01) |  | 0.50 (-0.06, 1.06) |  | 0.50 (-0.06, 1.06) |  | -0.84 (-1.70, 0.02) |  | 0.23 (0.01, 0.45)\* |
|  |  | 23'44'5-Penta-CB (#118) | 0.19 (-0.06, 0.45) |  | -0.38 (-0.70, -0.07)\* |  | 0.72 (0.12, 1.31)\* |  | 1.01 (0.21, 1.80)\* |  | -1.18 (-2.09, -0.26)\* |  | 0.27 (0.03, 0.51)\* |
|  |  | 2344'5-Penta-CB (#114) | 0.07 (-0.13, 0.26) |  | -0.06 (-0.31, 0.19) |  | 0.17 (-0.30, 0.64) |  | 0.23 (-0.41, 0.86) |  | -0.23 (-0.96, 0.50) |  | 0.12 (-0.07, 0.31) |
|  |  | 233'44'-Penta-CB (#105) | 0.22 (-0.03, 0.47) |  | -0.41 (-0.72, -0.10)\* |  | 0.68 (0.08, 1.27)\* |  | 1.00 (0.20, 1.79)\* |  | -1.18 (-2.09, -0.26)\* |  | 0.24 (0.00, 0.48)\* |
|  |  | 23'44'55'-Hexa-CB (#167) | 0.18 (-0.08, 0.45) |  | -0.31 (-0.65, 0.03) |  | 0.68 (0.05, 1.31)\* |  | 0.92 (0.08, 1.77)\* |  | -1.04 (-2.01, -0.06)\* |  | 0.29 (0.04, 0.54)\* |
|  |  | 233'44'5-Hexa-CB (#156) | 0.03 (-0.26, 0.33) |  | -0.12 (-0.50, 0.26) |  | 0.45 (-0.26, 1.16) |  | 0.57 (-0.39, 1.53) |  | -0.58 (-1.69, 0.52) |  | 0.26 (-0.02, 0.55) |
|  |  | 233'44'5'-Hexa-CB (#157) | 0.07 (-0.21, 0.35) |  | -0.19 (-0.55, 0.17) |  | 0.62 (-0.05, 1.28) |  | 0.82 (-0.07, 1.71) |  | -0.86 (-1.89, 0.18) |  | 0.28 (0.02, 0.55)\* |
| 　 | 　 | 233'44'55'-Hepta-CB (#189) | 0.06 (-0.20, 0.32) | 　 | -0.25 (-0.57, 0.08) | 　 | 0.61 (0.00, 1.21)\* | 　 | 0.90 (0.09, 1.71)\* | 　 | -0.96 (-1.90, -0.03)\* | 　 | 0.23 (-0.02, 0.47) |

Reproductive hormone levels and dioxin concentrations were loge-transformed and included in the model separately. Therefore, B (95% CI) in the Table is expressed as an e-fold increase in the cord blood hormone concentration for each e-fold increase in dioxin concentration. E2, estradiol; T, testosterone; DHEA, dehydroepiandrosterone; SHBG, sex hormone-binding globulin; PCB, polychlorinated biphenyl; PCDD, polychlorinated dibenzo-*p*-dioxins; PCDF, polychlorinated dibenzofuran.

Adjusted for maternal age, parity, smoking during pregnancy, alcohol consumption during pregnancy, blood sampling week during pregnancy, and annual income. aAdrenal androgen/glucocorticoid ratio = (DHEA and androstenedione)/(cortisol and cortisone)

\*p < 0.05, \*\*p < 0.01

Table S4. Adjusted linear regression coefficients (B) and 95% confidence intervals (CI) for reproductive and steroid hormone levels in cord blood in relation to dioxin-like congeners in maternal blood in males (pg/g lipids).

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 　 | 　 | 　 | LH | 　 | FSH | 　 | Inhibin B | 　 | INSL3 |
| 　 | 　 | 　 | B (95% CI) | 　 | B (95% CI) | 　 | B (95% CI) | 　 | B (95% CI) |
| Male | PCDDs | 1,2,3,7,8-Penta-CDD | -0.13 (-0.58, 0.32) | 　 | 0.04 (-0.29, 0.38) | 　 | -0.25 (-0.50, -0.01)\* | 　 | -0.11 (-0.29, 0.08) |
|  |  | 1,2,3,6,7,8-Hexa-CDD | -0.15 (-0.61, 0.32) |  | 0.08 (-0.26, 0.43) |  | -0.31 (-0.56, -0.06)\* |  | -0.12 (-0.32, 0.07) |
|  |  | 1,2,3,4,6,7,8-Hepta-CDD | 0.03 (-0.45, 0.52) |  | 0.03 (-0.33, 0.38) |  | -0.11 (-0.39, 0.16) |  | -0.01 (-0.21, 0.20) |
|  |  | OCDD | 0.02 (-0.44, 0.48) |  | 0.20 (-0.14, 0.54) |  | -0.23 (-0.48, 0.03) |  | 0.01 (-0.19, 0.21) |
|  |  |  |  |  |  |  |  |  |  |
|  | PCDFs | 2,3,4,7,8-Penta-CDF | 0.08 (-0.42, 0.58) |  | 0.34 (-0.02, 0.70) |  | -0.35 (-0.62, -0.08)\* |  | -0.08 (-0.30, 0.13) |
|  |  |  |  |  |  |  |  |  |  |
|  | Non-ortho PCBs | 33'44'5-Penta-CB (#126) | -0.10 (-0.37, 0.17) |  | 0.10 (-0.10, 0.30) |  | -0.23 (-0.38, -0.09)\*\* |  | -0.08 (-0.20, 0.03) |
|  |  | 33'44'55'-Hexa-CB (#169) | -0.14 (-0.52, 0.24) |  | 0.17 (-0.11, 0.45) |  | -0.32 (-0.52, -0.11)\*\* |  | -0.10 (-0.26, 0.06) |
|  |  |  |  |  |  |  |  |  |  |
|  | Mono-ortho PCBs | 2’344’5-Penta-CB (#123) | 0.06 (-0.25, 0.37) |  | 0.17 (-0.05, 0.40) |  | -0.16 (-0.33, 0.00) |  | -0.04 (-0.17, 0.09) |
|  |  | 23'44'5-Penta-CB (#118) | 0.05 (-0.30, 0.40) |  | 0.23 (-0.02, 0.49) |  | -0.23 (-0.42, -0.04)\* |  | -0.09 (-0.24, 0.06) |
|  |  | 2344'5-Penta-CB (#114) | 0.18 (-0.21, 0.57) |  | 0.25 (-0.04, 0.53) |  | -0.14 (-0.36, 0.07) |  | -0.07 (-0.23, 0.10) |
|  |  | 233'44'-Penta-CB (#105) | 0.03 (-0.29, 0.35) |  | 0.20 (-0.03, 0.43) |  | -0.24 (-0.41, -0.07)\*\* |  | -0.10 (-0.23, 0.04) |
|  |  | 23'44'55'-Hexa-CB (#167) | 0.13 (-0.26, 0.53) |  | 0.29 (0.00, 0.58)\* |  | -0.18 (-0.40, 0.04) |  | -0.09 (-0.26, 0.07) |
|  |  | 233'44'5-Hexa-CB (#156) | 0.21 (-0.25, 0.67) |  | 0.43 (0.11, 0.76)\*\* |  | -0.14 (-0.40, 0.12) |  | -0.08 (-0.27, 0.12) |
|  |  | 233'44'5'-Hexa-CB (#157) | 0.09 (-0.30, 0.49) |  | 0.17 (-0.12, 0.46) |  | -0.18 (-0.40, 0.04) |  | -0.10 (-0.27, 0.06) |
| 　 | 　 | 233'44'55'-Hepta-CB (#189) | 0.05 (-0.36, 0.46) | 　 | 0.11 (-0.19, 0.41) | 　 | -0.03 (-0.26, 0.20) | 　 | -0.06 (-0.23, 0.11) |

Reproductive hormone levels and dioxin concentrations were loge-transformed and included in the model separately. Therefore, B (95% CI) in the Table is expressed as an e-fold increase in the cord blood hormone concentration for each e-fold increase in dioxin concentration.

FSH, follicle stimulating hormone; INSL3, insulin-like factor 3; LH, luteinizing hormone; PCDD, polychlorinated dibenzo-*p*-dioxin; PCDF, polychlorinated dibenzofuran; PCB, polychlorinated biphenyl.

Adjusted for maternal age, parity, smoking during pregnancy, alcohol consumption during pregnancy, blood sampling week during pregnancy, and annual income.

\*p < 0.05, \*\*p < 0.01

Table S5. Comparison of the characteristics of included and excluded subjects in the study.

|  |  |  |
| --- | --- | --- |
| Characteristics | Included participants (n = 183) | Excluded participants (n = 320) |
| Maternal characteristics  |  |  |
|  Age at delivery (years) | 30.3 ± 4.7 | 30.4 ± 5.0 |
|  Pre-pregnancy BMI (kg/m2) | 21.2 ± 3.1 | 21.2 ± 3.3 |
|  Blood sampling weeks during pregnancy | 33.1 (31.3, 37.1) | 32.0 (30.9, 34.3)\*\* |
|  Parity |  |  |
| 0 | 100 (54.6) | 140 (43.8)\* |
| ≥1 | 83 (45.4) | 180 (56.3) |
|  Education level (years) |  |  |
| ≤12 | 78 (42.6) | 147 (45.2) |
| ≥12 | 105 (57.4) | 178 (54.8) |
|  Tobacco smoking during pregnancy |  |  |
| No | 148 (80.9) | 257 (79.1) |
| Yes | 35 (19.1) | 68 (20.9) |
|  Alcohol consumption during pregnancy |  |  |
| No | 119 (65.0) | 232 (71.4) |
| Yes | 64 (35.0) | 93 (28.6) |
|  Annual household income (million yen) |  |  |
| <5 | 124 (67.8) | 221 (68.6) |
| ≥5 | 59 (32.2) | 101 (31.4) |
| Infant characteristics |  |  |
|  Sex |  |  |
| Male | 85 (46.4) | 157 (48.9) |
| Female | 98 (53.6) | 164 (51.1) |
|  Gestational age at birth (weeks) | 39.4 ± 1.0 | 38.5 ± 1.7\*\* |
|  Birth weight (g) | 3133.2 ± 327.9 | 2984.8 ± 437.4\*\* |

Data are presented as the mean ± standard deviation, median (interquartile range) or n (%).

\*p < 0.05, \*\*p < 0.01 by Student’s *t*-tests and Chi-squared tests.