Children's Cohort Studies

Table 1. Studies Examining the Effects of Exposures to Environmental Pollutants: Methyl Mercury, PCBs, and Dioxins

No.	Study Name, Recruitment Period, Tracking Period	Country	Sample Size	Exposures	Outcomes	Principal Investigator	Summary	Conclusions
1	The Hokkaido Study of Environment and Children's Health (The Hokkaido Cohort Study) 2002–2005 Age 5–6 years	Japan	Approx. 20,000(focus study: n=514)	Endocrine disruptors (maternal blood, umbilical cord blood, breast milk, hair)	Congenital anomalies, birth weight, gestational age Allergies, neurodevelopmental and behavioral disorders	Hokkaido University	Prospective cohort for the purpose of monitoring congenital anomalies: particularly examination of risk factors for hypospadias and cryptorchidism, and sensitivity to endocrine disruptors	–
2	The Tohoku Study of Child Development 2001–2003 Age 6–7 years	Japan	Approx. 1,300	PCBs, methyl mercury, POPs, dioxins (mother's hair, maternal blood, umbilical cord blood, placenta, breast milk)	Effect on development (NBAS[1], KSPD[2], BSID[3], FTII[4], K-ABC[5], other)	Tohoku University	Examine the effects of perinatal exposures of persistent organic pollutants (POPs) on the development of children	–
3	The New Zealand Study 1980s Until age 6–7 years	New Zealand	238	Methyl mercury (mother's hair)	Effect on development (WISC-R[6], MCC[7], TOLD, other)	Kjellstrom et al. (1986,1989), no peer review Crump et al. (1998)	Study the effects of methyl mercury exposures on the development of children	At 4 years: A number of tests revealed a correlation between the concentration of methyl mercury in the mother's hair and negative effects on the development of the child. At 6–7 years: A negative correlation was observed if an extreme outlier (one case) of total mercury in the mother's hair was excluded. No negative correlation was observed if the outlier was included.

1 Neonatal Behavioral Assessment Scale
2 Kyoto Scale of Psychological Development
3 Bayley Scales of Infant Development
4 Fagan Test of Infant Intelligence
5 Kaufman Assessment Battery for Children
6 Wechsler Intelligence Scale for Children–Revised
7 Mother-Child Counseling

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4	The Seychelles Child Development Study 1984–1994 Until age 20 years (scheduled)	Republic of Seychelles	779	Methyl mercury (mother's hair)	Effect on development (WISC-III[8], CVLT[9], VIMI[10], BNT[11], WRAML[12])	Rochester University, WHO, Seychelles Ministry of Health (1986–)	Study the effects of methyl mercury exposures on the development of children	No negative effects were observed at 29, 66, and 107 months.
5	The Faroese Birth Cohort Study (Children's Health and the Environment in the Faroes—Cohort 1) 1986–1987	Faroe Islands (Denmark)	1,022	Methyl mercury, PCBs, lead, etc. (umbilical cord blood, hair)	Effect on development (WISC-R, CVLT, Bender-Gestalt Test, BNT)	Institute of Public Health (Denmark), The Faroese Hospital System	Study the effects of contaminants in seafood on the development of children	
	Study results available at current age of 14 years		878	Methyl mercury (umbilical cord blood, hair, blood)	Neurodevelopment			A significant correlation was observed between mercury concentrations in umbilical cord blood and both neuropsychological and neurophysiological testing results.
	(Cohort 2) 1994–1995		182	Methyl mercury, PCBs, DDEs, selenium (umbilical cord blood, hair, breast milk, maternal blood)	Neurodevelopment (NOS) Effect on thyroid gland hormones	Institute of Public Health (Denmark), The Faroese Hospital System	Same as above	A significant correlation was observed between concentrations of mercury in umbilical cord blood and decreases in NOS at postnatal week 2. At 7 years, concentrations of mercury in umbilical cord blood and mother's hair were observed to have a statistically significant effect on motor functions and language ability.
	(Cohort 3) 1998–2000		547	Methyl mercury, PCBs, etc. (umbilical cord blood, hair, maternal blood, breast milk)	Effect on neurodevelopment, immune system and endocrine system	Institute of Public Health (DK), The Faroese Hospital System	Same as above	Study terminated

8 Wechsler Intelligence Scale for Children—Third Edition
9 California Verbal Learning Test
10 Visual impairments and multiple impairments
11 Boston Naming Test
12 Wide-Range Assessment of Memory and Learning

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6	The Dutch PCB/Dioxin Study 1990–1992 Ongoing	Netherlands	418	PCBs (maternal blood, breast milk, umbilical cord blood, child's blood)	Physiological effect, effect on development	University of Groningen; Erasmus University Rotterdam; Agricultural University, Wageningen; TNO Nutrition and Food Research; TNO Medical Biological Laboratory; DLO State Institute for Quality Control of Agricultural Products	Study of thyroid gland hormone levels, intelligence, play behavior at school age, etc.	At 10–21days: A correlation was observed between medium and high levels of PCBs, PCDDs, and PCDFs in breast milk, and less optimal scores for neonatal development. At 3 months: A slight negative correlation was observed between concentrations of PCBs in pregnant women's blood plasma, and mental/motor development measured by Bayley Scales of Infant Development (BSID) scores. At 7 months: Medium and high levels of PCBs and dioxins in breast milk were observed to have a negative effect on BSID scores. At 42 months: A significant correlation was observed between fetal exposure to PCBs and low cognition scores.
7	The German Cohort Study 1992–1997 Age 3.5 years	Germany	171	PCBs (umbilical cord blood, breast milk)	Effect on development (BSID, Fagan visual recognition memory test)	Winneke et al.	Study the effects of maternal intake of PCBs on development of children	At 7 months: A significant correlation was observed between concentrations of PCBs in breast milk and mental development index.
8	The Oswego Newborn and Infant Development Project 1991–1994	USA	559	PCBs (records of maternal dietary intake of fish)	Effect on development	Lonky et al.	Study the effects of maternal intake of PCBs (from fish) on development of children	At 12–48 hours after birth: The group exposed to high concentrations of PCBs were linked to lower evoked responses and underdevelopment of autonomic nervous system, measured by Neonatal Behavioral Assessment Scale (NBAS). At 4.5 years (n=189): An association was observed between PCB concentrations in umbilical cord blood and increases in errors of commission measured by Continuous Performance Test (CPT), and decreases in the size of the splenium of the corpus callosum from MRI imaging.
	Study results available through ages 4.5 years, 8 years, and 9.5 years		189 202			Stewart et al.		At 8 and 9.5 years (n=202): An association was observed between concentrations of PCBs in umbilical cord blood and errors of commission measured by CPT. After 1.5 years, increases in errors of commission were observed to impair response inhibition.

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No.	Study Name, Recruitment Period, Tracking Period	Country	Sample Size	Exposures	Outcomes	Principal Investigator	Summary	Conclusions
9	The Michigan Cohort Study (Michigan/Maternal Infant Cohort Study) 1980–1981 Until age 11 years	USA	313	PCBs (umbilical cord blood, maternal blood)	Effect on development	Fein et al.	Study the effects of maternal intake of PCBs (from fish) on development of children	At 7 months (n=123): An association was observed between exposures to PCBs and lower responsiveness to visual recognition memory, measured by Pagan Test of Infant Intelligence (FTII). At 4 years (n=236): An association was observed between PCB concentrations in umbilical cord blood and lower test scores for language and short-term memory of quantities measured by McCarthy Scales of Children's Abilities (MSCA). At 11 years (n=212): An association was observed between fetal exposures to PCBs, and full-scale IQ and language IQ scores measured by Wechsler Intelligence Scale for Children (WISC-R).
10	The North Carolina Cohort Study (The North Carolina Breast Milk and Formula Project) 1978–1982 Until age 5 years	USA	912	PCB, DDEs, other	Effect on development, other	Rogan et al.	Prospective cohort study on general population	Neonatal period (n=867): An association was observed between the group exposed to high concentrations of PCBs in breast milk, and diminished muscle tone and reflexes measured by Neonatal Behavioral Assessment Scale (NBAS). An association was also observed between exposures to high concentrations of DDEs in breast milk and diminished reflexes. At 6 and 12 months (n=802): An association was observed between concentrations of neonatal exposures to DDEs and gross motor development (BPDI scores). A meaningful association was observed between concentrations of neonatal exposures to PCBs and BPDI scores. At 18 and 24 months (n=676, n=670): The group with the highest exposure was observed to have BPDI scale scores that were 4–9 points below mean scores. At 3, 4 and 5 years (n=506): No association was observed between exposures and MSCA scores.

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No.	Study Name, Recruitment Period, Tracking Period	Country	Sample Size	Exposures	Outcomes	Principal Investigator	Summary	Conclusions
11	German Environmental Survey (GerES) IV 2003–ongoing Until age 14 years	Germany	550	Lead, cadmium, mercury, organic chlorine compounds, IgE antibodies (blood) Stress markers (urine) House dust, drinking water, indoor air Noise	Hearing	German Federal Environmental Agency	Collect exposure data in various parts of Germany	–

Table 2. Studies Examining the Effects of Exposures to Environmental Pollutants: Lead

No.	Study Name, Recruitment Period, Tracking Period	Country	Sample Size	Exposures	Outcomes	Principal Investigator	Summary	Conclusions
12	Port Pirie Cohort Study 1978–1982 Into adulthood	Australia	831 (at recruitment) 537 (at age 4 years) 372 (at age 11–13 years)	Lead (blood)	Effect on development	McMichael, A.J. et al. (1988) Tong, S. (1996)	Recruitment of pregnant women in community situated near lead smelter	Lower IQ scores were observed among the high-exposure group. At 4 years, subjects with an average postnatal blood lead concentration of 1.50 µmol/lwere observed to have general cognitive scores that were 7.2 points below the mean (95% confidence interval, 0.3 to 13.2; mean score of 107.1). At 11–13 years, subjects whose average lifetime blood lead concentration increased from 10 to 20 µg/dl had IQ scores that were 3 points below the mean (95% confidence interval, 0.07 to 5.93).
13	Cincinnati Lead Study Cohort 1987–ongoing	USA	305 (at recruitment) 253 (at age 6.5 years)	Lead (blood)	Effect on development	Dietrich, K. et al. (1987) Dietrich, K. et al. (1993)	Recruitment of low-income mothers from neighborhoods with high risk of lead exposure	At both 3 and 6 months: A negative correlation was observed between children's blood lead concentrations and Bayley Scales of Mental Developmental Index (MDI) scores. At 6.5 years: Subjects with average lifetime blood lead concentrations over 20 µg/dl had WISC-R Performance IQ scores that were seven points lower than subjects under 10 µg/dl.
14	Boston Birth Cohort Study 1979–1981	USA	249 (at recruitment) 148 (at age 10 years)	Lead (blood)	Effect on development	Bellinger, D. C. et al. (1992)	Children born at Brigham & Women's Hospital (Boston, MA)	A correlation was observed between exposure levels at 2 years of age and lower WISC-R and K-TEA scores at 10 years. At 24 months, subjects with higher blood lead concentrations of 0.48 µmol/l (10 µg/dl) had WISC-R Full-Scale IQ scores that were 5.8 points below the mean (95% confidence interval, 1.7 to 9.9; P=0.007). The same subjects had K-TEA Battery Composite scores that were 8.9 points lower (95% confidence interval, 4.2 to 13.6; P=0.0003).
15	Christchurch Health and Development Study (CHDS) 1977 Tracked until age 21 years	New Zealand	1,265	Lead (teeth) One of a number of study items	Effect on mental and neurological development	Fergusson, D.M. et al. (1997) Fergusson, D.M. Horwood, L. J. (2001)	Residents of Christchurch, New Zealand	A negative correlation was observed between lead exposure levels detected in deciduous teeth shed at 6–8 years, and lower scores for word recognition. Lower-than-average scores were also observed at 18 years.
16	Cleveland Cohort Study	USA	160	Lead (maternal blood, umbilical cord blood, blood)	Effect on development	Ernhart, C.B. et al. (1989)	Low-income residents of Cleveland, Ohio	At five years, a clear association had not been established between blood lead concentrations and intelligence measured by Wechsler Preschool and Primary Scale of Intelligence (WPPSI) scores.

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No.	Study Name, Recruitment Period, Tracking Period	Country	Sample Size	Exposures	Outcomes	Principal Investigator	Summary	Conclusions
17	Mexico City Prospective Lead Study 1987–1992 Tracked until age 10 years	Mexico	157 (complete data at age 10 years: n=150)	Lead (blood)	Effect on development	Schnaas, L. et al. (2006)	Children born in Mexico City (part of cohort by National Institute of Perinatology)	An association was observed only between maternal blood lead concentration at 28 weeks gestation and lower recognition scores of children at 6–10 years, measured using Spanish-language version of Wechsler Intelligence Scale for Children.
18	Rochester Longitudinal Lead Study 1994–1995	USA	240	Lead (blood)	Effect on development	Canfield, R.L. et al. (2003)	Residents of Rochester, New York (part of large cohort to study and test effects of indoor dust management)	A significant negative correlation was observed between average lifetime blood lead concentration and IQ scores (P=0.004). For each increase of 1 µg/dl, IQ scores were 0.46 points lower. Blood lead concentrations were measured at 6, 12, 18, 24, 36, 48, and 60 months. IQ was tested at 3 and 5 years using Stanford-Binet Intelligence Scale.
19	The Yugoslavia Prospective Study of Environmental Lead Exposure 1985–1986	Yugoslavia	Recruitment of 1,502 mothers from two towns (900 from Pristina, 602 from K. Mitrovica) 577 children tracked until age 7.5 years	Lead (blood)	Effect on development, etc.	Factor-Litvak, P. (1999)	Residents of two towns in Kosovo, Yugoslavia	A correlation was observed between increases in blood lead concentration and lower scores on a variety of tests including for intelligence. Subjects with higher blood lead concentrations of 10–30 µg/dl had scores that were 2.5 points lower at 2 years (95% confidence interval, 0.2 to 4.8), 4.5 points lower at 4 years (95% confidence interval, 2.2 to 6.8), and 4.3 points lower at 7 years (95% confidence interval, 3.5 to 5.1). Subjects were tested using Bayley Scales of Mental Development Index (MDI) at 6, 12, 18, and 24 months, McCarthy Scales of Children's Abilities (MSCA) at 4 years, and Wechsler Intelligence Scale for Children-III (WISC-III) at 7 years.
20	Mothers and Children's Health and Environment (MOCHE) Study 2006–2010	South Korea	Recruitment of 500 mothers in first year only	Blood, biomarkers in urine (including lead, mercury, and cadmium) Environmental factors	Effect on development, allergies, eczema, asthma, etc.	Ha, E. (2007)	Three cities in South Korea	Based on preliminary results, an analysis of 300 subjects revealed a significant correlation between the blood lead concentration of mothers and femur length of their children. The correlation was not established for mercury levels.

Table 3. Large-Scale Studies on Exposures to Environmental Pollutants

No.	Study Name, Recruitment Period, Tracking Period	Country	Sample Size	Exposures	Outcomes	Principal Investigator	Summary
(1)	The National Children's Study 2008–2013 Until age 21 years	USA	100,000	• Natural and man-made environmental factors • Biological and chemical factors • Physical surroundings • Social factors • Behavioral influences • Genetic influences • Cultural and family influences • Geographic influences	Children's health • Asthma • Congenital anomalies • Development and behavior • Growth • Fertility and pregnancy	• U.S. Department of Health and Human Services (DHHS) • National Institutes of Health (NIH) • The Eunice Kennedy Shriver National Institute of Child Health and Development (NICHD) • The National Institute of Environmental Health Sciences (NIEHS) • Centers for Disease Control and Prevention (CDC) • U.S. Environmental Protection Agency (EPA)	• Tracking from prenatal to adulthood • Prospective cohort study implemented throughout the United States
(2)	The Norwegian Mother and Child Cohort Study (MoBa) 1999–2007 Until age 6 years	Norway	90,000 (from 1999 to September 2007)	• Health • Infection • Nutrition • Medication • Occupation • Lifestyle (alcohol, drugs, smoking, social status) • Banking of maternal blood and umbilical cord blood • Dietary survey, questionnaires	• Pregnancy (childbirth, eclampsia, premature birth, low birth weight, congenital anomalies) • Children (asthma, allergies, diabetes, cancer, polyarthritis, autism, ADHD)	• Norwegian Institute of Public Health	• Scheduled to track subjects from prenatal to age 6 years • Seeks to clarify the relationship between the health of Norwegian mothers and children, and environmental and genetic influences
(3)	Danish National Birth Cohort: Better Health for Mother and Child (BSMB) 1997–2002	Denmark	101,042 (1997–2002)	• No specific exposures set in advance • Banking of maternal blood and umbilical cord blood • Dietary survey, phone interviews with mothers	• Complications from pregnancy • Childhood disease from early exposure • Fetal development and determinants • Effect of medication and infectious disease, etc.	• Denmark Statens Serum Institut (Danish State Serum Institute)	• Improvement of prenatal care • Nested case-control investigation • Use of registries: natal treatment registries (illnesses during pregnancy, childbirth status, child body measurements), registry of special diseases (childhood cancer, childhood paralysis, diabetes, autism) • Clarify effects of disease infection, diet, genetic background and social environment on congenital anomalies, asthma, cancer and behavioral disorders in children, as well as testicular cancer and other pathologies in adulthood