

Table 2.10.1: Cohort studies on relationship of endocrine disruptors with infantile nerve development

Region and subjects	Number of subjects	Follow-up period	Compound	Route of exposure	Exposure indicator/concentration	Measurement	Age	Results
Severely exposed populations and highly polluted areas								
Japan								
Harada, 1976		1968	PCBs	Contaminated edible oil	Not	Not reported	Not reported	Prenatally exposed children showed low sensitivity, emotionlessness, low muscle tension and reduced intelligence.
Taiwanese yusho patients, Rogan, 1988 Chen, 1992, 1994		1979	PCBs,PCDFs	Contaminated edible oil	Mother and child sera	Cognitive development	4-7 Years	IQ consequently lower by 5 points No dependence on dose
Lai TJ ,2001	236 (118 exposed, 118 controls)					Bayley Scale of Infant Development (BSID): 6-30 months of age Binet IQ test: 30 months-5 years of age Raven's Color Progressive Matrices (CPM): 5-9 years of age Raven's Standard Progressive Matrices (SPM): from 9 years of age on	6 months-15 years	Exposed group showed scores in cognitive development tests lower than controls from 2 to 12 years of age.
Lai TJ ,2002	236 (118 exposed, 118 controls)					WISC-R Achenbach Child Behavior Checklist(CBCL) Rutter Child Behavior Scale A		Exposed group showed IQ lower than controls by 3 points (p = 0.05) Exposed group showed CBCL higher than controls by 3 points (p = 0.002); no effect of sex difference was observed. Exposed group showed Rutter behavior scale score higher than controls by 6 points (p < 0.001). Exposed children showed significant improvement by ageing for Rutter score only.
Michigan food chain(米国)								
Blank, 2000	327	1973-	PBBs	Accidental contamination				Severely exposed cases showed earlier menarche (11.6 years of age). Exposure to organohalogen via placenta or breast milk may affect start of puberty.
Spain								
Ribas-Fito,2003	92	1997-99	PCBs(28,52,101,118,138,15 HCB p,p'DDE	Area around of an electrochemical plant	Cord blood serum	BSID- II , Griffiths Scales	13 Months	Prenatal exposure to p,p'-DDE was correlated with delayed mental and motion development at 13th month. A double p,p'-DDE exposure level corresponded to decrease in mental development by 3.5 points and motion development by 4.01 points. Infants exposed to relatively high levels of p,p'-DDE and had short breast feeding periods showed low scores in both mental and motion development.
Population of pregnant women who took exposed fish								
Lake Michigan, U.S								
Newborns from fish-eating mothers	242	1980-81	PCBs	Contaminated fish	Maternal serum, cord blood serum, breast milk			
Newborns from non-fish-eating mothers	71							
Fein, 1984	242				PCB not detected in 70% of cord blood serum and 22% of maternal serum	Average concentration	Newborns	Body weight and head circumference disproportionately small for the length of gestation
Jacobson, 1985	123 white male 69 female 54				PCE in maternal serum 6±4 ng/mL in cord blood serum 3±2 ng/mL in breast milk 841±38 ng/g PBB in maternal serum 0±1 ng/mL in cord blood serum 3±4 ng/mL	Visual cognition Fagan Test	7 Months	Correlation dependent on exposure level (cord blood PCB level) with reduced responsiveness to stimulation No effect of postnatal exposure

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Jacobson, 1990	236				Breast milk 218±325 ng/g	Cognitive development, cognitive processing McCarthy scales of Children's Abilities	4 Years	Prenatally exposed infants showed exposure-dependent impairment of short-term memory in both language and numerical measures No effect of postnatal exposure
					Serum of children 4 years of age PCB 2±3 ng/ml PBB 0±1 ng/ml DDE 3±4 ng/ml		4 Years	Prenatal exposure associated with low perception-performance scores and impairment of short-term memory No effect of postnatal exposure
Jacobson, 1996	212				Serum of children 11 years of age PCB 1±1 ng/ml PBB 0±0 ng/ml DDE 1±1 ng/ml	WISC-R	11 Years	Prenatal exposure significantly correlated with low scores in the entire test and linguistic IQ No effect of postnatal exposure
Jacobson, 2002	Breast feeding for less than 6 weeks: 56 Breast feeding for 6 weeks or more: 122				Cord blood serum 2.6±2.0ng/mL(N=144) Maternal serum 5.7±3.6ng/mL(N=158) Breast milk 829.7±384.3ng/g of fat(N=124)	McCarthy scales of Children's Abilities WISC-R		
Jacobson, 2003	4 Years of age: 154 11 Years of age: 148				Cord blood serum 2.7±2.1ng/mL(N=117) Maternal serum 5.9±5.9±3.8ng/mL(N=128) Breast milk 859.3±388.2ng/g of fat(N=107)	58 4 Year of age: sustained attention, working memory 11 Year of age: concentrated attention, sustained attention, executive function, working memory, Seashore rhythm test, mental rotation reaction time	4 and 11 years	Deleterious effects observed chiefly in children not breast-fed Prenatal PCB exposure correlated with higher impulsiveness, poorer attention and poorer visual and aural working memory for children not breast-fed Disorder of visual space or hyperactivity not observed
Oswego, New York, U.S. Infants from 162 women not eating Lake Ontario fish Infants from 141 women eating Lake Ontario fish Lonky, 1998		1991-94	PCBs, HCB PCDDs dieldrin, lindane chlordane cadmium mercury mirex	Contaminated fish	None	Nerve and behavioral development	12-48hr	Severely exposed newborns showed weaker reflex and immature autonomous nerve system
Stewart, 2000						(NBAS)	25-48hr	Concentration of highly chlorinated PCBs significantly correlated with poorer habituation and autonomous nerve stability
Stewart, 2003	212 38 Months of age: 194, 54 months of age: 197		PCBs, MeHg		PCBs in cord blood, MeHg in hair	McCarthy scales of Children's Abilities	38 and 54 months	Significant correlation of GCI (general cognitive index) and cord blood level of highly chlorinated PCBs observed at 38th month, but not at 54th month, after adjustment for confounders

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Stewart, 2003	189		PCBs		Cord blood PCBs	continuous performance test(CPT)→ Michigan Catch the Cat test MRI Scanning	4.5 Years	Dose-dependent correlation found between cord blood PCB level and CPT commission errors Commission errors correlated with the size of corpus callosum (r = 0.20), but not of other brain domains; correlation clearer for smaller callosal sizes
General populations								
North Carolina (美国)								
Rogan, 1986	912/930	1978-82	PCBs,DDE		Maternal serum, cord blood, breast milk, placenta	Behavioral development (NBSA)	Neonates	Severe trans-placental exposure to PCB associated with lower muscle tension and reflex Severe trans-placental exposure to DDE associated with lower reflex
Gladen, 1988	802					Psychomotor development Bayley Scale of Infant Development(BSID)	6 and 12 months	Severe trans-placental exposure to PCB associated with low psychomotor score, but not with intelligence score, at the 6th and 12th month Postnatal exposure via breast milk not associated with Bayley score Trans-placental DDE exposure showed no consequent effect
Rogan&Gladen, 1991						Psychomotor development Bayley Scale of Infant Development(BSID)	18 and 24 months	Prenatal PCB exposure associated with retarded motor development up to the 24th month Postnatal exposure via breast milk not associated with test score DDE exposure showed no consequent effect
Rogan&Gladen, 1991	506					Psychomotor development McCarthy scales of Children's Abilities	3, 4 and 5 years	Changes in development observed in prenatally exposed babies disappeared by late infancy Boys transplacentally exposed to high-level DDE showed higher body heights and weights in adolescence
Gladen, 2000	594							
Rotterdam and Groningen, Holland								
Huisman, 1995	418		PCBs,PCDDs PCDFs	Contaminated products (including oils)	Maternal blood, cord blood, breast milk	Neurobehavioral development	10-21 Days	PCB levels in maternal and cord blood not associated with neurological dysfunction Exposure to high-level PCBs, PCDDs or PCDFs in breast milk associated with low muscle tension, without remarkable neurological effects
Huisman, 1995						Neurobehavioral development Bayley Scale of Infant Development(BSID)	18 Months	Prenatally exposed infants showed significant impairment of nerve functions Slight correlation with breast milk level
Koopman-Esseboom, 1996						Psychomotor development Bayley Scale of Infant Development(BSID)	3, 7 and 18 months	Prenatal PCB exposure slightly lowered neurobehavioral score at 3 months of age Exposure to PCBs and dioxins via breast milk impaired neurobehavioral development at 7 months of age Intelligence development at 7 months of age affected positively by breast feeding, impaired by prenatal exposure to PCBs or dioxins
Lanting, 1998	394					Neurobehavioral development Touwen/Hempe	42 Months	Pre- or postnatal or immediately past exposure had no effect

Region and subjects	Number of subjects	Follow-up period	Compound	Route of exposure	Exposure indicator/concentration	Measurement	Age	Results
Patandin, 1999	395					Cognitive development Kaufman Assessment Battery for Children	42 Months	Prenatal PCB exposure associated with low cognition scores Postnatal and immediately past exposure has no effect at the 42th month
Vreugdenhil, 2003	372		Maternal blood, cord blood: PCB 118, 138, 153, 180 Breast milk: 17 dioxins, 6 dioxin-like PCBs, 20 non-dioxin-like PCBs			McCarthy scales of Children's Abilities	6-7 Years	Prenatal exposure to PCBs and dioxins adversely affected the cognitive and motion performance of children grown in less-than-standard parents or home environment.
		Breast-fed: 194, artificially fed: 178						
Vreugdenhil, 2003	158					Pre-School Activity Inventory(PSAI): Evaluation of playing behavior	7.5 Years	Effects of prenatal PCB exposure as estimated by maternal and cord blood level on masculine and androgynous behavior scores were significantly different between boys and girls (p < 0.05) Boys' scores in the masculine scale (p = 0.042 for maternal blood level and p = 0.001 for cord blood level) and the androgynous scale (p = 0.011 for cord blood level) showed significant association of PCB exposure with decreased masculine behavior in playing. Girls' scores in the androgynous scale (p = 0.048 for maternal blood level) showed significant association of PCB exposure with increased masculine behavior in playing. Prenatal exposure to dioxins was significantly associated with increased feminine behavior in playing in the feminine scale for both boys and girls (p=0.048).
		Breast-fed: 85 (53 males, 32 females)						
Vreugdenhil, 2004	83					Neuropsychological tests (Rey Complex Figure Test, SRTT, Auditory-Verbal Learning Test, Tower of London)	9 Years	Prenatal exposure to high-level PCBs associated with longer reaction time, greater variation of reaction time, and lower Tower of London scores
		Low exposure: 42, high exposure: 41						
Vreugdenhil, 2004	83					ERPs (P300)		High exposure group showed longer P300 latency than low exposure group PCB exposure via breast milk not associated with P300 latency Infants breast-fed for more than 16 weeks showed shorter P300 latency than those breast-fed for 6-16 weeks or artificially fed P300 amplitude not associated with perinatal PCB exposure or breast feeding
Germany								
Winneke, 1998	171		PCBs		Average cord blood level 0.55ng/ml Average breast milk level 427ng/gfat	Neurological optimum Cognitive-motion development	10-20 Days 7 Months	No effect on nerve development No significant effect
Winneke, 2002	171		PCB(138,153,180)		Cord blood, breast milk, infant blood (42nd month)	BSID-II, Kaufman scale, HOME (18th month)	7,18, 30 and 42 months	Breast milk PCB level in significant inverse association with psychomotor development at the 30th and 42nd month Effects of PCB exposure via breast milk discerned at the 42nd month Home environment showed positive effects from the 30th month on

Region and subjects	Number of subjects	Follow-up period	Compound	Route of exposure	Exposure indicator/concentration	Measurement	Age	Results
U.S. Daniels JL, 2003	1207	1959-65	PCBs (28,52,74,101,105,118,138,153,170,180,194,203)		Maternal serum: 3.1 μ g/l on an average	BSID	8 Months	No association observed between serum PCB level and infant's mental and physical development (MDI and PDI) (MDI: β =0.1, p =0.71, PDI: β =0.5, p =0.14)
Italy Riva E, 2004	25	2000	PCB(105, 118, 138, 153, 156, 180) DDT DDE		Breast milk (2 days, 1 month and 3 months after delivery)	Visual evoked potential (VEP) P100	12 Months	P100 latency for stimulation at a visual angle of 60 minutes associated with DDT (r = 0.513) and PCB (r = 0.504) levels VEP latency at 15 min associated with colostral level of DDT, DDE and all PCBs except PCB105 (r = 0.401-0.618) Partial correlation factor between colostral PCB 180 and P100 latency at 15 min was 0.403 (p = 0.07) after controlling for C22:6 n-3 A weak association was thus established between impaired visual function at 12 months of age of healthy infants and the levels of PCBs, DDT and DDE in colostrum.

Table 2.10.2: Synchronic study on relationship of endocrine disruptors with infantile nerve development

Region and subjects	Number of subjects	Compound	Route of exposure	Exposure indicator/concentration	Measurement	Age	Results
Perera,2003 U. S.							
African-Americans	116	Polycyclic aromatic hydrocarbons (PHA)	Indoor atmospheric PHA	African-Americans:0.6ng/mL Dominicans:0.5ng/mL	Outcome on birth	On birth	Prenatal exposure to high-level PAHs significantly associated with low body weight (p = 0.003) and low head circumference (p = 0.01) on birth after adjustment for confounders CPF significantly associated with reduced body weight and height on birth for all subjects (p = 0.003, 0.01), body weight on birth for African-Americans (p = 0.04) and body height on birth for Dominicans (p < 0.001); no change of the results by adjustment
Dominicans	146	Environmental tobacco smoke (ETS): conitine concentration Organophosphate pesticide: chlorpyrifos (CPF)	Maternal blood plasma conitine level	African-Americans:3.5ng/m3 Dominicans:3.9ng/m3	Body weight, height and head circumference on birth		
			Plasma CPF level	African-Americans:8.0pg/g Dominicans:7.1pg/g			

Table 2.10.3: Case-control study on relationship of endocrine disruptors with infantile nerve development

Region and subjects	Number of subjects	Compound	Route of exposure	Exposure indicator/concentration	Measurement	Age	Results	
Ruckart,2004 U. S.								
Children from Mississippi and Ohio exposed/unexposed to methyl parathion	Exposed group: (MP) 132 unexposed group: 147	Methyl parathion	Illegal use of organophosphate pesticides for insect control	MP from houses PNP in urine	Mississippi exposed group: MP $\geq 150 \mu\text{g}/\text{cm}^2$ or PNP $\geq 100 \text{ppb}$ Ohio exposed group: MP $\geq 132.9 \mu\text{g}/\text{cm}^2$ or PNP $\geq 100 \text{ppb}$ Mississippi unexposed group: MP $< 25 \mu\text{g}/\text{cm}^2$ Ohio unexposed group: MP $< 35 \mu\text{g}/\text{cm}^2$ or MP = 0, PNP $< 25 \text{ppb}$ Highly exposed group: MP $\geq 1000 \mu\text{g}/\text{cm}^2$ or PNP $\geq 300 \text{ppb}$	Pediatric Environmental Neurobehavioral Test Battery Performance-based tests Informant-based tests	7 Years and later	Exposed children showed more difficulties in tests on short-term memory and attention than unexposed children Parents of exposed children reported more frequently about their children's behavioral and physical problems than parents of unexposed children

Table 2.10.4: Ecological study on relationship of endocrine disruptors with infantile nerve development

Region and subjects	Number of subjects	Compound	Route of exposure	Exposure indicator/concentration	Measurement	Age	Results
Dorner G, 2002 (Member countries of PISA Study)							
15 year-old students born in 1984-85		DDT		Total DDT in breast milk	Mental competence (reading, 15 Years writing, math, science)		Significant inverse correlation between total DDT level in breast milk and PISA International score (p < 0.001) Significant inverse correlation between total DDT in breast milk and mental competence of 15 year-old students from 10 countries in 3 continents as well as 14 German states in PISA International and PISA National (2000) (P < 0.001) Significant correlation between total DDT in breast milk and ratio of mentally retarded children in German states in 1984-85 (p < 0.001)