IMMUNOLOGICAL EFFECTS OF BACKGROUND EXPOSURE TO POLYCHLORINATED BIPHENYLS AND DIOXINS IN DUTCH TODDLERS

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Background
Prenatal exposure to polychlorinated biphenyls (PCBs) and dioxins is associated with changes in the T-cell lymphocyte population in healthy Dutch infants[1]. We investigated whether these changes persist into later childhood and whether background exposure to PCBs and dioxins is associated with the prevalence of infectious or allergic diseases and humoral immunity at toddler age.

Methods
The original study group consisted of 207 healthy mother-infant pairs. Prenatal exposure to PCBs and dioxins was estimated by the sum of PCBs 118, 138, 153 and 180 (ΣPCB) in maternal and cord plasma and in breast-fed infants by the dioxin, planar PCB and mono-ortho PCB toxic equivalent (TEQ) levels in human milk. At 42 months of age, body burden was estimated by the ΣPCB in plasma. The prevalence of infectious and allergic diseases was assessed by a parent questionnaire. Humoral immunity was measured by antibody titers for mumps, measles and rubella after primary vaccination. In a subgroup of children immunological marker analyses of lymphocytes were done.

Results
Adjusted for confounders a higher ΣPCB maternal was associated with less shortness of breath with wheeze. For the ΣPCB cord results were in the same direction but not significant. Current PCB body burden was associated with a higher prevalence of recurrent middle ear infections and of chickenpox and a lower prevalence of allergic reactions (Table 1). This effect of current PCB body burden was only significant in breast-fed and not in formula fed children and was counteracted by the duration of breastfeeding in infancy. Of the 21 children with recurrent middle ear infections 9 (10.7%) were formula fed, 6 (13.6%) were breast-fed for less and 6 (12.8%) for more than 16 weeks; of the 130 children with chickenpox 58 (69%) were formula fed, 36 (81.8%) were breast-fed for less and 36 (76.6%) for more than 16 weeks; and of the 14 children with allergic reactions 8 (9.5%) were formula fed, 2 (4.5%) were breast-fed for less and 4 (8.5%) for more than 16 weeks. In addition the dioxin TEQ had a significant effect on coughing, chest congestion and phlegm (OR 1.06, 95%CI 1.00-1.11, p=0.04) and the mono-ortho and planar PCB TEQ had a significant effect on recurrent middle ear infections (mono ortho PCB TEQ; OR 1.17, 95%CI 1.04-1.32, p=0.01, planar PCB TEQ; OR 1.10, 95%CI 1.00-1.20, p=0.04).

Table 1: Prevalence of infectious and allergic diseases and effects of prenatal and current PCB body burden

	Prevalence	Prenatal PCB exposure ΣPCB Maternal		Current PCB body burden ΣPCB 42 months	
	n (%)	Odds ratio (95% CI)[a]	p-value	Odds ratio (95% CI)[a]	p-value
Infectious diseases					
Recurrent middle ear infections (6 or more episodes)	21 (12.0%)	1.37 (0.87-2.17)	0.17	3.06 (1.17-7.98)	0.02*
Pneumonia	5 (2.9%)	0.41 (0.10-1.63)	0.21	0.01 (0.01-29.68)	0.13
Scarlatina	13 (7.4%)	1.00 (0.56-1.80)	0.98	0.59 (0.08-4.03)	0.59
Chickenpox	130 (74.3%)	1.43 (0.92-2.24)	0.11	7.63 (1.21-48.54)	0.03*
Other infectious diseases	15 (8.6%)	1.04 (0.60-1.82)	0.87	0.85 (0.27-2.67)	0.79
Allergic diseases					
Eczema	42 (24.0%)	1.18 (0.82-1.71)	0.37	0.92 (0.41-2.08)	0.84
Allergic reaction	14 (8.0%)	0.62 (0.29-1.32)	0.22	0.01 (0.01-0.37)	0.01*
Asthma or bronchitis	30 (17.1%)	0.87 (0.55-1.40)	0.56	0.38 (0.06-2.57)	0.32
Coughing, chest congestion, or phlegm lasting for 10 days or more[1]	48 (27.4%)	1.08 (0.75-1.54)	0.69	1.12 (0.58-2.16)	0.74
Attacks of shortness of breath with wheeze[1]	17 (9.7%)	0.44 (0.18-0.99)	0.05*	0.34 (0.02-4.49)	0.41

[1] in the previous 12 months *significant at the ≤.05 level[a] corrected for gender, early feeding type (breast-fed or formula fed), duration of breastfeeding during infancy (6 to 16 or more than 16 weeks), parity (firstborn or second born), maternal education and parental occupation (low), tobacco smoking by one or both parents (yes or no) , family history of atopy in one or more parents (yes or no) and day care or nursery school attendance of the child (yes or no)

Median antibody levels for mumps were 94.3 U/ml (range 2.9-2334.1), for measles were 1.2 IU/ml (range 0.08-12.0) and for rubella were 47.0 IU/ml (range 4.3-220.0). After logarithmic transformation antibody levels to mumps were negatively correlated with ΣPCB maternal levels (Pearson correlation -0.17, p=0.04) and antibody levels to rubella were negatively correlated with ΣPCB cord levels (Pearson correlation -0.19, p=0.03) . There were no significant correlations between antibody levels and the dioxin, planar and mono-ortho PCB TEQ levels nor with the ΣPCB at 42 months of age.

Prenatal PCB exposure was associated with an increased number of CD8+ (cytotoxic), CD4+CD45RO+(memory), TcR αβ+ and CD3+HLA-DR+ (activated) T cells (Table2). Results were significant in the formula fed and not in the breast-fed group. There were no significant correlations between the results of the white blood cell counts and immunological marker analyses and the dioxin, planar and mono-ortho PCB TEQ levels nor with the ΣPCB at 42 months of age.

Table 2: Results of the white blood cell counts and the immunological marker analysis (n=85) in relation to prenatal PCB exposure

	Absolute counts			Prenatal PCB exposure			
	Percentiles, 10^9/L			ΣPCB maternal		ΣPCB cord	
White blood cells	p5	p50	p95	Pearson correlation[1]	p-value	Pearson correlation[1]	p-value
Monocytes	0.3	0.5	0.9	0.04	0.73	0.09	0.43
Granulocytes	2.2	4.1	7.5	0.14	0.22	0.15	0.20
Lymphocytes	2.2	4.1	6.6	0.25	0.02*	0.22	0.05*
T-cell markers							
CD3+	1.4	2.7	4.6	0.25	0.02*	0.21	0.07
CD3+CD4+	0.8	1.7	2.7	0.19	0.08	0.16	0.17
CD3+CD8+	0.4	0.9	1.7	0.27	0.01*	0.24	0.04*
CD4+CD45RA+	0.3	1.0	1.9	0.12	0.26	0.04	0.77
CD4+CD45RO+	0.2	0.4	0.6	0.25	0.02*	0.26	0.02*
TcR αβ+	1.1	2.5	4.2	0.25	0.02*	0.20	0.08
TcR γδ+	0.1	0.2	0.4	0.17	0.12	0.15	0.20
CD3+HLA-DR+	0.1	0.3	0.5	0.26	0.02*	0.31	0.005*
B-cell markers							
CD 19/20+	0.4	0.9	1.7	0.12	0.28	0.15	0.20
NK-cell markers							
CD16+ and/or CD56+/CD3-	0.1	0.3	1.1	0.13	0.23	0,11	0.31

[1] after logarithmic transformation
*significant at the ≤.05 level

Conclusion

In Dutch toddlers the effects of perinatal background exposure to PCBs persist into childhood and might be associated with a greater susceptibility to infectious diseases. Common infections acquired early in life may prevent the development of allergy and therefore PCB exposure might be associated with a lower prevalence of allergic diseases.

References

1. Weisglas-Kuperus N, Sas TC, Koopman-Esseboom C, et al. Immunologic effects of background prenatal and postnatal exposure to dioxins and polychlorinated biphenyls in Dutch infants. *Pediatr Res* 1995;**38**(3):404-10.

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