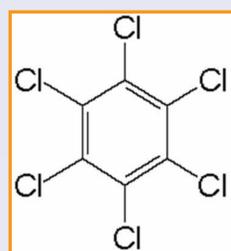


# Exposure to Hexachlorobenzene During Pregnancy and Social Behavior at Age 4 Years

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## Background



- Hexachlorobenzene (HCB) is an organochlorine chemical that has been used in agriculture and industrial processes.
- Behavioral impairment after HCB exposure has been described in animal models but little information is available in humans.
- Unusually high atmospheric concentrations of HCB were found in the population of a rural village of 5000 inhabitants in the vicinity of an electrochemical factory (Flix, Ribera d'Ebre, Spain) (Sala et al. 1999).

Adult inhabitants studied in 1994 had the highest serum HCB levels ever found (mean of 36.7 ng/mL) (To-Figueras et al. 1997) and levels of HCB in the cord serum of newborns from this population studied in 1999 were among the highest ever reported (Sala et al. 2001).

- High concentrations of HCB were also found in newborns from Menorca (Carrizo et al. 2006). Menorca is one of the Balearic Islands in the northwest Mediterranean Sea, which has no local pollution sources.

## Objectives

- Our aim in this study was to follow up the children from the Ribera d'Ebre and Menorca cohorts to assess the association of prenatal and postnatal exposure to HCB and social behavior of children at age four.

## Population and methods

- Two birth cohorts in Ribera d'Ebre and Menorca (Spain) were set up between 1997-1999 (n=475).
- The California Preschool Social Competence Scale (CPSCS) (Levine et al. 1969) and the Attention-Deficit Hyperactivity Disorder Criteria of Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association 2000) were scored by each child teacher.
- Organochlorine compounds were measured in cord serum.
- Children's diet and parental sociodemographic information was obtained through questionnaire.

## Results

- Children from the Ribera d'Ebre cohort were more likely to be an only child and to have been breastfed for shorter periods, their mothers were less educated and were more likely to have a lower social class and to drink and smoke during pregnancy.
- Concentrations of HCB were, as expected, higher in Ribera d'Ebre but the maximum values were higher in Menorca (Table 1).
- The crude behavioral evaluation was equal in both cohorts (the frequency of a low social Competence scoring was 19% in Ribera d'Ebre and 23% in Menorca; the frequency of ADHD was 15% in Ribera d'Ebre and 16% in Menorca).
- The Social Competence and the ADHD checklist were highly correlated. Those children without ADHD symptoms had a mean (SE) score in the California test of 95.21 (0.58) while those children with ADHD symptoms had a mean (SE) score of 76.18 (1.34).
- Those children with concentrations of HCB above 1.5 ng/ml at birth had a statistically significant increased risk (relative risk (95% CI) of having a poor Social Competence = 4.04 (1.76-9.58) and ADHD = 2.71 (1.05-6.96)) (tables 2 and 3).
- No association was found between HCB and the cognitive and psychomotor performance of these children.

**Table 1. Distribution (median and centiles 25 and 75) of HCB in cord serum (ng/ml) by cohort**

	n	Minimum	Centile 25	Median	Centile 75	maximum
Total	475	0.14	0.48	0.73	1.13	9.82
Ribera d'Ebre	70	0.17	0.80	1.13	1.69	5.77
Menorca	405	0.14	0.46	0.68	1.02	9.82

**Table 2. Crude and adjusted relative risk of having a scoring < 80 points in the Social Competence scale at age four in relation to in utero exposure to HCB**

	Unadjusted n=377 Coefficient (95% CI)	Adjusted <sup>c</sup> n=377 Coefficient (95% CI)
HCB category		
Reference <sup>a</sup>	1	1
0.5-0.99 ng/ml	1.16 (0.62-2.18)	1.40 (0.68-2.87)
1-1.49 ng/ml	1.04 (0.48-2.29)	1.47 (0.59-3.62)
≥ 1.5 ng/ml	2.88 (1.39-5.97)*	4.04 (1.76-9.58)*
HCB, ng/ml <sup>b</sup>	1.52 (1.05-2.22)*	1.79 (1.15-2.76)*

\* p<0.05; \*\* p<0.10

a Reference group: <0.5 ng/ml

b Natural logarithmic transformed HCB concentration

c Adjusted for age, cohort, gender, maternal education, paternal education, tobacco and alcohol exposure, maternal age in years and type and duration of breastfeeding

**Table 3. Crude and adjusted relative risk of having ADHD symptoms at age four in relation to in utero exposure to HCB**

	Unadjusted n=377 Coefficient (95% CI)	Adjusted <sup>c</sup> n=377 Coefficient (95% CI)
HCB category		
Reference <sup>a</sup>	1	1
0.5-0.99 ng/ml	1.19 (0.58-2.42)	1.23 (0.54-2.78)
1-1.49 ng/ml	1.73 (0.77-3.91)	2.28 (0.88-5.96)
≥ 1.5 ng/ml	2.05 (0.90-4.67)**	2.71 (1.05-6.96)*
HCB, ng/ml <sup>b</sup>	1.49 (0.99-2.24)**	1.63 (1.02-2.63)*

\* p<0.05; \*\* p<0.10

a Reference group: <0.5 ng/ml

b Natural logarithmic transformed HCB concentration

c Adjusted for age, cohort, gender, maternal education, paternal education, tobacco and alcohol exposure, maternal age in years and type and duration of breastfeeding

## Conclusions

- Prenatal exposure to current concentrations of HCB in Spain is associated with a decrease in the behavioral competence at preschooler ages.
- These results should be considered when evaluating the potential neurotoxicological effects of HCB.

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