SET-UP OF CRITICAL PCB BODY BURDEN VALUES

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Introduction

PCBs or polychlorinated biphenyls were used in the industry, as a mixture, for their insulating properties (electrical transformers) and their chemical and physical stability (inks, paints). Their production and use were gradually reduced through the 1970s before finally being banned in 1987. Chemically stable and of low biodegradability, these molecules are classified as persistent organic pollutants.
Highly lipophilic, PCBs gradually accumulate in the food chain, becoming particularly concentrated in the fatty tissues of animals. As a result, the foods with the highest PCB levels are foods of animal origin with high fat content, such as oily fish in contact with contaminated sediment and milk, dairy products and eggs. Consequently, food is the main contamination route for the general population (over 90% of total exposure).
They are slowly eliminated (over several years) through stools. They are also found in mother's milk and blood lipids, where they are measured. PCB toxicity is mainly linked to the accumulation in the body over time (body burden). This means that occasional exposure to these molecules through a highly contaminated food will have limited effect on health. High PCB exposure (accidental discharges, work-related exposure) may trigger skin reactions (chloracne, pigmentation of the nails and skin), eye reactions (hypersecretion) and liver problems (transitory changes in hepatic enzyme activity). For lower, chronic exposure levels, the most alarming manifestations associated with PCBs are neuro-behavioural effects, which have been observed in young children who were heavily exposed to PCBs during pregnancy and breastfeeding. Other effects have been reported in adults: metabolic disturbances, thyroid conditions.
The agency for food, environmental and occupational health and safety (Anses) received a request from the Directorate General for Health, for an opinion on interpreting the health impact of PCB concentration levels. This expertise was based on the review of the most recent and comprehensive results available in the literature.

Materials and methods

Data were available from the National Public Health Institute of Quebec (INSPQ) and the PCBRisk project from Slovakia (http://www.pcbrisk.sk).
In 2007, the National Public Health Institute of Quebec conducted a critical review of epidemiological studies published since 1997 (1) to analyze the causal relationships between exposure to PCBs (assessed in terms of levels in the body, which are estimated in most of these studies, by measuring the PCBs in plasma lipids and in maternal milk) and the incidence of health problems in exposed subjects. Dose-response relationships have been researched by correlating markers of exposure with markers of effects.
In Europe, Eastern Slovakia is particularly contaminated with PCBs due to historical pollution related to the presence (particularly in the Michalovce District) of a chemical factory releasing large quantities of PCBs into nearby rivers for 25 years (1959-1984). The Slovak PCBRISK Project (http://www.pcbrisk.sk) is the most comprehensive European epidemiological study, in terms of range of exposure and PCB concentration levels, for establishing relationships between PCB levels in the body and the occurrence of health effects after chronic exposure to low doses in both adults (2047 individuals) and children aged 8-9 years (434 individuals) (2, 3, 4, 5, 6 and 7). In this cohort, 15 PCB congeners were measured: PCB 28, 52, 101, 105, 114, 118, 123, 138, 153, 156, 157, 167, 170, 180, and 189.

On top of these two above mentioned studies, the European food safety agency (EFSA)[1] also published some reference values in humans.

Results and discussion:

1) Critical effects in humans.

INSPQ. This review of the literature highlighted great variability in the results observed from one study to another and/or in the same cohort, and in particular:

- inconsistencies regarding causal relationships between perinatal exposure to PCBs and the disruption of immune parameters in children,
- lack of a relationship between perinatal exposure to PCBs and the incidence of upper airway infections in children aged under five years,
- lack of a relationship between exposure to PCBs and female fertility,
- the existence of contradictory relationships between exposure to PCBs and male fertility (see changes in sperm parameters) making it impossible to establish a maximum biological level without effect on humans, to date,
- lack of any effect of PCBs on neurological function (manual stability and/or mnemic functions) of subjects aged 50 to 90 years (consumers or non-consumers of fish) whose PCB concentration levels are lower than 1900 ng of total PCB/g of plasma lipids.

However, from this analysis it is apparent that the critical health effects most often reported in humans are:

- effects on mental and motor development in children exposed *in utero*,
- effects on the endocrine system (particularly the thyroid).

PCBRisk. In the most heavily exposed adults, the observed effects consist of:

- changes in the parameters for functional exploration of the thyroid: thyroid volume, elevated anti-thyroperoxidase antibodies, change in level of thyroid hormones and thyrotropin (Langer *et al.*, 2009),
- disturbances of glucose metabolism (8),

In children (particularly vulnerable during the prenatal period and lactation) the effects observed were:

- impairment of mental and motor development (hyperactivity, sensorimotor abilities and memory, etc.),
- hearing problems (measured by different functional screening tests appropriate for children), defective dental enamel formation.

EFSA. In its Opinion of 8 November 2005, suggested a BMDL of approximately 1000 ng total PCB / g of plasma lipids (P_o=0.05 and BMR=0.05) for the entire population. This conclusion was based on BMDLs of 630-710 ng total PCB /g of lipids and 1200-3000 ng total PCB /g of lipids respectively, established on the basis of cognitive and immunotoxic effects observed in children exposed to PCBs *in utero* (9).

2) Conclusion

Regarding, pregnant women or women of childbearing age, as well as lactating women, the three reports converge to accept a critical concentration level of 700 to 1000 ng total PCB /g of maternal plasma lipids. This value corresponds to the level of prenatal PCB body burden above which the occurrence of significant effects on the mental and motor development of children exposed *in utero* cannot be ruled out.
Regarding the other population categories, various relationships have been described between exposure to PCBs (in terms of levels in the body) and changes in the physiological parameters related to reproductive, endocrine and immune function. However, the heterogeneity of the results across the different studies failed to clearly establish a causal relationship. Consequently, Anses proposed a value of 700 ng total PCB /g of plasma lipids as

[1] EFSA: European Food Safety Authority. Opinion of the scientific panel on contaminants in the food chain on a request from the commission related to the presence of non dioxin-like polychlorinated biphenyls (PCB) in feed and food. The EFSA Journal 2005; 284:1-137.

the critical concentration threshold for pregnant women, women of childbearing age, lactating women, and children less than three years of age. Due to the persistence of PCBs in the body and thus the gradual increase in concentration levels with age, this threshold value also applies to young and adolescent girls. In boys over three years of age, adult men, and women past childbearing age, the data are fragmentary and even contradictory, making clinical interpretation difficult.

Given that,

- variations in thyroid hormones reported in the PCBRISK study occur in individuals with PCB levels in the body higher than 2300 ng total PCB /g of plasma lipids, and that
- the results reported by Schantz *et al.* (10), in subjects aged 50 to 90 years(consumers or non-consumers of fish) indicate that below 1890 ng total PCB /g of plasma lipids, the effect of PCBs on neurological function (manual stability and/or mnemic functions) can be excluded,

Anses suggested, for information purposes, the value of 1800 ng total PCB /g of plasma lipids as the critical concentration level for the rest of the population (boys over three years of age, adult men, and women over 45 years).

	Women < 45 years	Women > 45 years	Men < 45 years	Men > 45 years
Critical concentrations in humans (ng total PCB / g of plasma lipids)	700	*1800**	*1800**	*1800**

**Value given for information purposes regarding results available in adults*

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