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## The effects of exposure to environmental chemicals on child development

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# CHAPTER 1

## **General introduction and outline**

Sietske A. Berghuis



## INTRODUCTION

The studies contained in this thesis provide insight into the effects of exposure to environmental chemicals on child health, with a focus on neurological and hormonal development up to and including adolescence.

### Environmental chemicals

In the past decades, various classes of chemicals were produced that were used in a wide variety of consumer products, such as coolants in electrical appliances and flame retardants in a range of household items. Two examples of such chemicals are polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs). These compounds have proved useful as flame retardants on account of their resistance to high temperatures.

After two incidents with PCB-contaminated rice oil, awareness of the potential toxic effect of exposure to PCBs increased,<sup>1,2</sup> while concern about PBDEs arose after the observation that these chemicals had been found in measurable quantities in the environment and in human biota.<sup>3</sup> Chemicals like PCBs and PBDEs are known as persistent organic pollutants (POPs) because they continue to exist in the environment for long periods on account of their resistance to chemical and biological degradation.<sup>4</sup> On account of the growing concern about their toxicity and persistence, the production and use of several POPs has recently been reduced or banned altogether.

PCBs belong to a class of chemicals consisting of 209 different congeners with varying numbers of chlorine atoms attached to a biphenyl at varying positions. They were produced between 1929 and 1985 and used in a variety of products including coolants in heat-transfer systems, lubricants in plastics and flame-retardants.<sup>5</sup> PCBs are metabolized in the human body by hepatic microsomal oxidases to form hydroxylated metabolites (OH-PCBs).

Polybrominated diphenyl ethers (PBDEs) belong to a class of chemicals consisting of 209 different congeners with a varying number of bromine atoms attached to a diphenyl ether at varying positions. Since the 1970s, PBDEs have been extensively used in, for example, electronic equipment and many other consumer products.<sup>6</sup> Since the 1990s, the production and use of penta PBDE congeners has been voluntarily banned in Europe. In 2006, the use of penta and octa PBDEs in electrical and electronic equipment were restricted by a European Union directive.<sup>7</sup> At international level, during the Stockholm Convention in 2009, commercial penta and octa PBDEs were listed as POPs and rules were introduced to eliminate these compounds (Decisions SC4/14 and SC4/18).<sup>8</sup>

### **Exposure to POPs**

On account of their resistance to biological and chemical degradation exposure to POPs continues even after their production and use was banned. PCBs are still released into the environment through the use and disposal of products containing PCBs that were produced before the ban. For humans the main routes of exposure to PCBs are through ingesting contaminated food and through inhaling contaminated air.<sup>9, 10</sup> PCBs accumulate in the food chain and are stored in fatty tissue. Therefore, the main sources of dietary exposure to PCBs is through eating fish, meat and dairy products. Inside dwellings the concentration of PCBs can rise as a result of their leaking from household appliances, such as televisions and refrigerators, or on account of PCBs contained in construction materials, such as caulk and flame retardant coatings.<sup>9, 10</sup>

Exposure to PBDEs is also ongoing, mainly through eating contaminated food and through inhaling dust.<sup>6</sup> The main route of exposure to PBDEs in North-America appears to be through inhaling dust, while ingesting food is the more important route in Europe. Differences in the production and use of commercial PBDEs might be the reason for the differences in exposure levels and predominant exposure pathways between continents. Residents of North-America, for example, have higher levels of PBDEs in their blood compared to the residents of Europe.<sup>6</sup>

Environmental chemicals, such as PCBs and OH-PCBs, are transferred from mother to fetus during pregnancy, thus exposure to these toxic compounds already occurs prenatally.<sup>11</sup> Considering that the prenatal period is a sensitive period during which essential developmental processes take place, exposure to environmental chemicals might have great and permanent consequences for outcomes in later life. Evidence exists that fetuses and children are more susceptible to the harmful effects of PCBs and PBDEs than adults.

### **Effects on neurological development in childhood**

With regard to the neurological development of children, there is a growing body of evidence that even low-level environmental exposure to several POPs, including PCBs and PBDEs, might have neurotoxic effects. This topic is elaborated in **Chapter 2**.

### **Endocrine disrupting effects**

Several environmental chemicals have endocrine disrupting effects and, as a consequence, affect hormonal development in children.<sup>12</sup> These so-called endocrine disruptors might interfere with normal hormonal and metabolic pathways by, for example, mimicking or antagonizing the effects of hormones. Because thyroid hormones are essential for the developing brain, disturbances of thyroid hormone metabolism might be an underlying mechanism for the neurotoxic effects of endocrine disruptors. Apart from the effects on thyroid hormone metabolism, PCBs and OH-PCBs seem to also have estrogenic and anti-

estrogenic effects. Because puberty is the period during which major hormonal changes take place, endocrine disruptors might impair normal pubertal development in adolescents.

## AIMS

Our primary aim was to determine whether prenatal exposure to POPs was associated with the neurological functioning at the age of 3, 18 and 30 months, and with neuropsychological and behavioral outcomes in adolescence. Our secondary aim was to determine whether prenatal exposure to POPs was associated with hormonal processes, including thyroid hormone metabolism, and pubertal development.

## OUTLINE

### **Part 1. The neurotoxic effects of exposure to environmental chemicals during childhood: an overview**

In Part 1, **Chapter 2**, we provide an overview of recent literature on the neurotoxic effects of POPs on outcomes during childhood.

### **Part 2. Exposure to environmental chemicals and neurological functioning from birth up to and including adolescence**

Part 2 focuses on the effects of prenatal exposure to PCBs on neurological functioning up to and including adolescence. In **Chapter 3** we describe the effects on the spontaneous motor repertoire of three-month-old infants. In addition, neurological functioning was also assessed at three months of age. The effects of prenatal exposure to PCBs and OH-PCBs on neurological functioning are presented in **Chapter 4**. In **Chapter 5** we describe the effects on the motor and mental development in infants at the age of 18 and 30 months. The last assessment of neurological functioning was performed during adolescence, including neuropsychological tests and parental questionnaires on the behavior of their adolescents. In **Chapter 6** we investigate whether prenatal exposure to PCBs and OH-PCBs affect the neuropsychological outcomes of 13 to 15-year-old adolescents.

### **Part 3. Endocrine disrupting effects of environmental chemicals**

In Part 3 we focus on the endocrine disrupting effects of environmental chemicals. On account of the fact that several environmental chemicals might interfere with normal hormonal processes, they might affect the development of children. Because thyroid hormones play an important role in the development of the central nervous system, we

investigated whether PCBs and OH-PCBs might interfere with thyroid hormone levels in cord blood and in infants at 3 months and 18 months of age. In **Chapter 7** we address the question whether disruption of thyroid hormone metabolism is a possible underlying mechanism of the toxicity of PCBs and OH-PCBs. Pubertal development is a process during which changes in hormone levels play an important role, and some chemicals might interfere with sex hormone metabolism. Therefore, we also determined the effects of prenatal exposure to environmental chemicals on pubertal development and report on them in **Chapter 8**.

In **Chapter 9** we provide a general discussion that integrates the results of the studies included in the separate chapters, and we point out some future perspectives. In **Chapter 10** we summarize our findings in English and Dutch.

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