Commentary: Halogenated organic compounds and child’s growth: a growing public health problem

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Halogenated organic compounds (HOCs) such as polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethylene (DDE) may interfere with normal hormonal function and, thereby, affect growth and maturation. Thus, these toxicants were termed ‘endocrine disruptors’. Two outcomes, easily observed and frequently linked to HOCs, are birth size and post-natal height and growth. Both outcomes can indicate adverse intrauterine and post-natal development and are associated with several adult diseases. A number of studies have reported that DDE and PCBs are associated with reduced birth sizes and with children’s height and growth (Table 1). Surprisingly, for clearly defined birth size measures, it has not yet been determined whether DDE, PCBs, or other HOCs are responsible for the effects. In addition, new endocrine disruptors are emerging. Furthermore, among the various PCB congeners, it is not clear which of these or which group

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Table 1: Studies on exposure to HOCs and height/growth of children

<table>
<thead>
<tr>
<th>Authors</th>
<th>Sample size, sex</th>
<th>Exposure</th>
<th>Exposure time window</th>
<th>Outcome time window</th>
<th>Outcome</th>
<th>Girls</th>
<th>Boys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pless et al.</td>
<td>109 girls, 112 boys</td>
<td>Estimated intake of PCDD and PCDF in the diet</td>
<td>Childhood</td>
<td>Birth, 1, 4, 7, months, 1, 2, 4 years</td>
<td>Growth</td>
<td></td>
<td>PCDD/PCDF: growth ↓</td>
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<tr>
<td>Guo et al.</td>
<td>118 exposed 117 controls</td>
<td>PCBs and PCDF in utero vs control</td>
<td>Prenatal</td>
<td>11–14 years</td>
<td>Height</td>
<td>?</td>
<td>PCBs/PCDF: height ↑</td>
</tr>
<tr>
<td>Patandin et al.</td>
<td>207 children</td>
<td>PCDD, PCDF, PCBs</td>
<td>Prenatal</td>
<td>Birth—3 months</td>
<td>Growth: difference</td>
<td>PCDD/PCDF: ↑</td>
<td></td>
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<tr>
<td>Gladen et al.</td>
<td>316 girls, 278 boys</td>
<td>Estimated intake of DDE via breast milk</td>
<td>Infancy</td>
<td>Height at puberty, 10–15 years</td>
<td>Height</td>
<td>PCB: growth ↓</td>
<td></td>
</tr>
<tr>
<td>Karmas et al.</td>
<td>175 girls, 125 boys</td>
<td>PCBs and DDE serum blood levels in children 7–11 years</td>
<td>Prenatal/childhood</td>
<td>Birth, 1, 3.5, 6.5 months, 1, 2, 4, 8,9,10 years</td>
<td>Growth</td>
<td>DDE: growth ↓; PCB: –</td>
<td></td>
</tr>
<tr>
<td>Blank et al.</td>
<td>308 daughters</td>
<td>Estimates of maternal PBBs and PCB serum levels</td>
<td>Prenatal and post-natal</td>
<td>5–24 years</td>
<td>Height</td>
<td>–</td>
<td>&lt; &gt;</td>
</tr>
<tr>
<td>Gladen et al.</td>
<td>304 boys</td>
<td>Prenatal DDE and DDT</td>
<td>Prenatal</td>
<td>10–20 years, each year</td>
<td>Height</td>
<td>&lt; &gt;</td>
<td>–</td>
</tr>
<tr>
<td>Hertz-Picciotto et al.</td>
<td>211 girls, 188 boys</td>
<td>Prenatal PCBs</td>
<td>Prenatal</td>
<td>Birth, 5 years</td>
<td>Growth: difference</td>
<td>PCB: growth ↓</td>
<td></td>
</tr>
<tr>
<td>Lamb et al.</td>
<td>41 girls, 109 boys</td>
<td>Prenatal PCBs, ortho-substituted</td>
<td>Prenatal</td>
<td>Birth, 4, 7, 17 years</td>
<td>Height, growth</td>
<td>–</td>
<td>PCB: height &amp; growth ↑</td>
</tr>
<tr>
<td>Ribas-Fito et al.</td>
<td>873 girls 909 boys</td>
<td>Prenatal PCBs and DDE</td>
<td>Prenatal</td>
<td>1, 4, 7 years</td>
<td>Height, growth</td>
<td>DDE: height ↓</td>
<td>PCB: –</td>
</tr>
</tbody>
</table>

DDE, dichlorodiphenyl dichloroethylene; PCDD, polychlorinated dibenzo-dioxins; PCDF, polychlorinated dibenzofurans; PBBs, polybrominated biphenyls; PCBs, polychlorinated biphenyls; ↓, decrease; ↑, increase; – no effect; < >, not measured/does not apply.
(e.g. ortho vs non-ortho substituted PCBs, Table 1) is the culprit. There may be evidence for most HOCs, but the mechanisms are still unknown.

In contrast to birth size, childhood height and growth exhibit more complexity (Table 1): height is based on one measurement, growth on at least two height determinations. Based on the presented studies, the critical time window of exposure may either be prenatal, post-natal, or both. Some investigations were based on exposure measurements of only one HOC and did not control for others. Height measurements were taken only in infancy, before or after puberty, or span childhood and adolescence. Since HOCs may exert sexually dimorphic effects in children, some analytical approaches include a stratification by sex. The study by Núria Ribas-Fitó et al. in this issue is, to date, the largest and most comprehensive assessing the effects of multiple prenatal exposures (PCBs and DDE) on height and growth while stratifying by sex and race. The authors presented evidence that prenatal DDE exposure may reduce prepubertal height. One surprising finding is that African American children seem to be more susceptible. This in turn raises suspicions that genetic polymorphisms of some unknown mechanisms may explain existing contradictory findings.

Given that HOCs are ubiquitous, biomagnified in the food chain, and bring to bear a variety of adverse effects, the gap in our knowledge is alarming. In addition, newly emerging toxicants exhibiting potentially endocrine disrupting effects are being produced in large amounts (e.g. phthalates, polybrominated diphenyl ethers). There are several possible explanations and approaches to better characterize HOCs and, consequently, protect public health from current and future risks.

Disquieting explanations include epigenetic effects and inheritance. Given a unique composition of DNA, gene activity may vary. A change in gene activity (expressed or silenced) may occur through modifications of either the structure of the double strand helix (by methylation) or of histones (by acetylation, methylation, or phosphorylation). Alterations in gene activity could be modulated by HOCs. If such epigenetic modifications occur during early fetal life, they may be retained through cell division and, thereby, passed on to future generations.

Hence, reduced height in a girl may be due to exposure to HOC in her grandmother. The study setting reported by Núria Ribas-Fitó et al. would facilitate such an investigation.

On the other hand the puzzle of contradictory findings seems to be a result of lack of collaboration in a world of belligerent competition for funding. For instance, three of the nine reports in Table 1,28,30,11 all having contradictory findings, originated from the same Collaborative Perinatal Project in the US. Hence, for the sake of the common good we need to convene, sort out problems, rerun analyses, and develop scientific, sound strategies to better protect the vulnerable public.

References

21 Newbold RR, Padilla-Banks E, Jefferson WN. Adverse effects of the model environmental estrogen diethylstilbestrol are transmitted to subsequent generations. Endocrinology 2006;147:511–17.


