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Persistent organic pollutants and semen quality: The LIFE Study

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HIGHLIGHTS

- Chemicals in each of four classes of POPs associated with semen quality.
- Associations indicate both positive and negative effects on semen quality.
- POPs at environmentally relevant levels associated with semen quality.
- PBDEs 17, 28 and 153 associated with higher percentage of abnormal sperm morphology.
- OCPs and PCBs associated with lower DNA stainability, morphometry and morphology.

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ABSTRACT

Growing evidence suggests that persistent environmental chemicals such as polychlorinated biphenyls may adversely affect human fecundity. The purpose of this study was to evaluate associations between persistent environmental chemicals and semen quality among 501 male partners of couples discontinuing contraception for purposes of becoming pregnant. Men provided a blood specimen and two fresh semen samples collected approximately a month apart that underwent next day analysis for 35 semen quality endpoints. Serum samples were analyzed for 36 polychlorinated biphenyls (congeners #18, 28, 44, 49, 52, 66, 74, 87, 99, 101, 114, 118, 128, 138, 146, 149, 151, 153, 156, 157, 167, 170, 172, 177, 178, 180, 183, 187, 189, 194, 195, 196, 201, 206, 209); 1 polybrominated biphenyl (#153); 9 organochlorine pesticides; and 10 polybrominated diphenyl ethers (congeners #17, 28, 47, 66, 85, 99, 100, 153, 154183) using high resolution mass spectrometry. To estimate the effect of chemicals on semen quality, we regressed each semen marker on each chemical while adjusting for research site, age, body mass index, serum lipids, and cotinine levels. Males with chemical concentrations in the fourth quartile, as compared to the first quartile, showed significant associations for several individual chemicals in each chemical class and type of semen quality parameter indicating negative and positive associations with semen quality. Polybrominated diphenyl ethers in particular were associated with several measures of increased abnormal morphology. These exploratory results highlight the role of environmental influences on male fecundity, and are of particular interest given the ubiquitous exposures to these compounds.
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Abbreviations: β-HCH, β-hexachlorocyclohexane; DDE, 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene; DDT, 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane; γ-HCH, γ-hexachlorocyclohexane; HCB, hexachlorobenzene; LIFE Study, Longitudinal Investigation of Fertility and the Environment Study; LOD, Limit of Detection; OCPs, organochlorine pesticides; PBB, polybrominated biphenyl; PBDEs, polybrominated diphenyl ethers; PCBs, polychlorinated biphenyls; POPs, persistent organic pollutants.

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1. Introduction

Growing evidence suggests that persistent environmental chemicals such as polychlorinated biphenyls (PCBs) may adversely affect human fecundity, though few prospective couple-based cohort studies have been conducted. Much concern has been raised regarding the reproductive health consequences of exposure to persistent organochlorine pollutants (POPs) as PCBs and dichlorodiphenyltrichloroethane (DDT) in particular have been associated with reduced sperm motility (Toft et al., 2006; Rignell-Hydbom et al., 2004; Bonde et al., 2008), and concentration (Haugen et al., 2011), as well as reduced couple fecundity (Buck Louis et al., 2013). Moreover, these chemicals have been shown to readily penetrate the blood-testis barrier (Bush et al., 1986), which may alter endocrine homeostasis and impact testicular function. Although these chemicals have also been quantified in seminal fluids, little information has been reported on what these chemical concentrations may mean for reproductive function. Studies relating serum chemical concentrations and semen quality have been limited, however, in that they typically only evaluate a select number of PCBs with a basic semen analysis that focuses only on sperm count, motility, and morphology, and in some cases DNA fragmentation, despite modern technology to evaluate additional functional measures that have been related to fecundity.

Therefore, the objective of this study was to explore potential associations between multiple POPs in serum including polybromated biphenyl (PBB), organochlorine pesticides (OCPs), polybrominated diphenyl ethers (PBDEs), and PCBs, and a comprehensive semen quality assessment in a population based prospective cohort study. These hypotheses are of great interest given the widespread exposure to environmental chemicals and the need for human research at environmentally relevant doses.

2. Materials and methods

2.1. Design and study population

The LIFE Study was a prospective cohort study designed to investigate environmental influences on human fecundity and fertility, and its design and methods were described previously in detail (Buck Louis et al., 2011). In brief, 501 male partners of couples discontinuing contraception for the purposes of becoming pregnant were recruited from 16 counties in Michigan and Texas from 2005 to 2009 using sampling frameworks tailored for each State allowing for the identification of couples planning pregnancy in the near future. Eligible men were aged 18+ years in a committed relationship; were able to communicate in English or Spanish; and were not surgically or medically sterile. Full human subjects' approval was granted from all participating institutions prior to obtaining informed consent from all participants.

2.2. Data collection

Upon enrollment, in-person interviews were conducted with each male partner to ascertain health, demographic, and reproductive histories. All data and biospecimens were collected in the home, and baseline interviews were followed by a standardized anthropometric assessment for determination of body mass index (BMI) conducted by research nurses (Anthropometric Standardization Reference Manual, 1988). The research nurse obtained non-fasting blood (~10 mL) for quantification of serum chemicals and lipids using equipment determined to be free of the contaminants under study. Samples were transported on ice to the site laboratories for processing, and remained frozen at −20 °C or colder until shipment on ice to the laboratory.

2.3. Serum POP measurements

All analyses were conducted by the Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, using established protocols for the quantification of POPs in serum. Chemicals included (a) 1 PBB (PBB 153); (b) 9 OCPs [hexachlorobenzene (HCB), β-hexachlorocyclohexane (β-HCH), γ-hexachlorocyclohexane (γ-HCH), oxychlordane, trans-nonachlor, mirex, p,p′-dichlorodiphenyltrichloroethane (p,p′-DDT) and its metabolites p,p′-dichlorodiphenyldichloroethylene (p,p′-DDE) and o,p′-DDT]; and (c) 10 PBDEs (congeners 17, 28, 47, 66, 85, 99, 100, 153, 154, and 183); (d) 36 PCBs (congeners 28, 44, 49, 52, 66, 74, 87, 99, 101, 105, 110, 114, 118, 128, 138, 146, 149, 151, 153, 156, 157, 167, 170, 172, 177, 178, 180, 183, 187, 189, 194, 195, 196, 201, 206, and 209). Serum concentrations are reported in nanograms per gram of serum (ppb) and were measured using isotope dilution gas chromatography-high-resolution mass spectrometry using previously published procedures (Kuklenyik et al., 2005; Sjodin et al., 2004). We did not substitute by any constant for concentrations below the limit of detection or perform lipid standardization in order to minimize bias associated with these approaches when interested in estimating health effects (Richardson and Ciampi, 2003; Schisterman et al., 2005, 2006). Serum levels of cotinine were quantified using liquid chromatography-isotope dilution tandem mass spectrometry (Bernert et al., 1997) for assessment of baseline exposure to smoking with cut-points based on previous literature (Pirkle et al., 2006; Wall et al., 1988). Serum lipids were quantified using commercially available enzymatic methods (Akins et al., 1989), and reported as total serum lipids (nanograms per gram of serum) using established calculation methods using individual components (Phillips et al., 1989).

2.4. Semen collection and analysis

A baseline semen sample was obtained followed by a second sample approximately one month apart irrespective of couples' pregnancy status. Men collected semen samples through masturbation without the use of any lubricant following a recommended two days of abstinence using home collection kits (actual abstinence time: median 3.0 d, mean 4.1 d) (Royster et al., 2000; Turner and Schrader, 2006). At collection, a glass capillary tube was placed into the semen, and each subject recorded the duration of abstinence, time of semen collection and any information regarding sample collection loss or spillage. Semen samples were shipped via Federal Express overnight to the study's andrology laboratory at the National Institute for Occupational Health and Safety for analysis representing next-day analysis. Semen delivered to a central andrology laboratory by overnight mail in insulated mailing kits have been successful in maintaining specimens for other studies (Royster et al., 2000; Luben et al., 2007; Olshan et al., 2007). Semen analysis after home collection has been reported to be reliable for all semen parameters with the exception of motility parameters (Morris et al., 2003; Stovall et al., 1994). A percentage of sperm are alive after 24 h and a next-day motility assessment still can be made and may provide important information on sperm function and survivability (Stovall et al., 1994).

We quantified 35 semen parameters including five reflecting general characteristics (volume, straw distance, sperm concentration, total sperm count, hypo-osmotic swollen), eight motility measures, 12 morphometry measures, 8 morphology measures, and two sperm chromatin stability assay measures, using established laboratory protocols inclusive of ongoing quality assurance and control procedures (American Society of Andrology, 1996). Of note is that some parameters are a compilation of other parameters. Specifically, sperm concentration is equal to total sperm

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