Effects of Prenatal Exposure to Phthalates

Laurie A. Johnson, ME-PD, MS Ed.

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Abstract

The purpose of this review of literature is to examine the association of phthalate exposure with development. Phthalates are chemical compounds used in poly-vinyl chloride, PVC; vinyl flooring, cosmetics, shampoo, air fresheners, soft plastic items, intravenous tubing, food packaging and wraps, textiles, paints, cleaning products and detergents. The effects of phthalates on fetuses, newborns, infants, toddlers, school-aged children and adult subjects have been extensively researched. Multiple studies examined associations between phthalate exposure and physiological, cognitive and behavioral development of the subjects. The review of research examines the history of toxic chemical legislation, beginning with the 1976 Toxic Substances Control Act and the role of regulatory agencies in the United States, including the Environmental Protection Agency, EPA; the Consumer Product Safety Commission, CPSC; and the Food and Drug Administration.

Keywords: phthalates, developmental toxicants, cognitive function, obesogen, phthalate syndrome, executive function

There are several types of environmental pollutants that can act as prenatal teratogens, affecting the development of the fetus. According to Santrock (2011), the word teratogen is derived from the Greek word *tera*, which means monster. One of the most studied environmental teratogens today is the group of chemicals called phthalates, pronounced /tha- lates/. In the United States phthalates are primarily used as agents in producing polyvinyl chloride (PVC), according to the EPA (2012). The research of Kim et al., (2011) stated that phthalates in PVC products can be released into the atmosphere, acting as an "indoor pollutant" (p.2). The EPA action plan (2012) noted that phthalates can also be absorbed into the skin from children's toys and medical devices including intravenous tubes and blood bags. In addition, the EPA discussed the inclusion of phthalates in "plastics, paints, wood varnishes and [use in] lacquers, cosmetics…textiles, propellants, food packaging, dental materials and paper" (p. 3). The National Resources Defense Council, NRDC, added adhesives, dyes, inks, cleaning products, detergents, and pharmaceutical products to the list.

The United States Environmental Protection Agency (EPA) in its revised action plan (2012) outlined the agency's intent to investigate the "manufacturing, processing, distribution in commerce, and /or use of [these] eight phthalates" (p.1) According to the EPA, two other federal agencies, the Consumer Product Safety Commission (CPSC) and the Food and Drug Administration (FDA) monitor phthalate concentrations. The FDA is responsible for examining phthalate levels in plastic food containers and wraps, cosmetics, and medical items including intravenous tubing and bags.

Janssen (2010) reported that the 1976 Toxic Substances Control Act, TSCA, was passed to provide safety of chemicals from production through disposal. Janssen further stated that TSCA needs to be reformed, citing the possible impact of phthalates on human development.

Janssen (2010) stated that "Since 1999 six phthalates (BBP, DBP, DEHP, DiNP, DnOP, and DiDP) have been restricted for use in toys in the EU and at least 14 other countries have banned these phthalates in children's toys. The EU has also banned the use of DEHP, BBP, and DBP in cosmetics." (p. 2). In 2005 the European Commission mandated the elimination of the phthalates "DEHP, DBP and BBP in all toys and childcare articles…[and] DINP, DIDP and DNOP were banned from use in toys and childcare articles, if they can be put in the mouth by children" (EPA, 2012, p.10).

According to Janssen (2010), the National Toxicology Program, NTP, "…concluded that BBP, DBP, DEHP, DiDP, and DnHP [all] were reproductive or developmental toxicants" (p. 2). Engel et al., (2010) reported that in 2008 the United States passed legislation to regulate the allowable level of DEHP, DBP and benzylbutyl phthalate in "bath toys or other small plastic toys that can be placed in the mouth easily" (p. 2). Engel et al. also stated that studies have not determined if the unregulated, replacement phthalates could have potentially harmful effects. In 2012 two of the compounds on NTP's toxicant list, DiDP and DnHP, remain unregulated. The states of California, Maine, Washington, and Vermont have developed regulations for the concentration of phthalates in children's items.

Janssen (2010) noted that because of loopholes in the 1976 Toxic Substances Control Act, the FDA has not been successful in regulating the widespread use of phthalates in products that "… may disrupt the body's hormones, causing reproductive health effects" (p. 10).

Janssen (2010) stated that in 2008 the National Academy of Sciences, (NAS), noted that humans regularly absorb multiple types of phthalates. NAS requested that the EPA analyze "phthalate toxicity using a cumulative risk assessment approach" (p. 2). Janssen further noted that "seven

phthalates of concern (DEHP, DBP, BBP, DiBP, DiDP, DiNP and DnOP) are found in the majority of Americans tested" (p. 1).

Janssen (2010) discussed Walgreen's voluntary removal air fresheners from its stores as a result of NRDC data on the possible hazards of specific phthalates. S.C. Johnson agreed to remove its air fresheners and cleaning products that contained phthalates, and now "publicly discloses the chemical ingredients in its products" (p. 1) . Due to the lack of regulation, Janssen stated "The specific types and quantities of phthalates used in individual products is not publicly available information and phthalates often do not appear on product labels" (p. 2)

Engel et al., (2010) noted that phthalate levels can be measured through urine, blood, amniotic fluid and breast milk. Urinalysis is the primary procedure utilized in prenatal phthalate research. The same study noted that the evidence of phthalates in urine can remain for "days to months" (p. 2).

Kim et al., (2011) reported initial research with laboratory animals exposed to phthalates appeared to indicate an associated impairment of reproductive development in the animals' offspring. Kim et al. also discussed the hyperactive and erratic behavior of rats born after fetal exposure to phthalates.

Based on previous animal testing, Kim et al., (2011) researched the effects of prenatal phthalates, administering Mental and Psychomotor Development Indices, (MDI, PDI) assessment from the Bayley Scales of Infant Development. The results indicated a relationship between phthalate exposure and lower MDI and PDI in six month old subjects. Kim noted an association between phthalate exposure and the brain's regulation of the "thyroid hormone system…or the lipid signal transduction pathways that may influence the development of cognitive function" (p. 10).

Engel et al. (2010) conducted research on the association of prenatal phthalate exposure on behavior and executive function of subjects four to nine years of age. The study was initiated after previous research and studies reported a relationship between prenatal phthalate exposure and infant cognitive development. Parents of the subjects completed the standardized "Behavior Rating Inventory of Executive Function (BRIEF), and the Behavior Assessment System for Children-Parent Rating Scales (BASC-PRS)" (Engel et al., 2010, p.4).

The researchers discussed an association between fetal exposure to phthalates and clinically significant externalizing behaviors, commonly known as "acting out" behaviors, including attention deficit hyperactivity disorders and the more serious conduct disorders. Similarly Whyatt's research (2012) noted a relationship between prenatal phthalate exposure and behavioral, cognitive and motor development in three year old subjects.

Philippat et al., (2012) researched the relationship between prenatal phthalate exposure and birth weight, noting that the phthalate 2,4-DCP and 2,5-DCP were associated with low birth weight. Conversely the study reported that elevated BP3 in the mother's urine was linked to a significant increase in birth weight of males exposed to BP3 in utero.

In (2010) Hatch studied the relationship between phthalates and body mass index (BMI) and waist circumference (WC) of males aged twenty to fifty-nine. Hatch found that higher levels of phthalates appeared to increase the males' BMI and WC while lowering the BMI of females in the same age group. Hatch described phthalates as *obesogens* because of their potential impact on androgen function.

Swan's 2005 studies of male subjects, aged two to thirty-six months, reported an association between phthalate concentration, testicular development and descent, and shortened distance between the subjects' genitals and anus. Swan also stated that in studies with laboratory rats, the

virility of the rats declined. Swan's 2010 research referred to *phthalate syndrome* (p.1) to describe the reduction in the distance between the anus and genitals of laboratory canine subjects and under- developed testicles of human subjects who were exposed to phthalates in utero.

The EPA action plan (2012) noted the relationship between phthalates and "the reproductive development effects…shortened anogenital distance observed in newborn boys; and shortened pregnancy, lower sex and thyroid hormones, and reduced sperm quality observed in adults," (p. 4) The same report noted that "…in adult life [and that] people are exposed to several phthalates at once." (p. 4).

Despite the discussion of such associations, the EPA noted that "only two [phthalates](DBP and DEHP) of the 8 phthalates are listed on EPA's Toxics Release Inventory (TRI) list of toxic chemicals" (p.6). The term "toxic" was not defined in the report.

Many of the studies of the effects of phthalates have been replicated in other research. People of all ages can be exposed to several phthalates at one time. Although some action has been taken to protect children, there are still questions and concerns about what needs to be done to keep these teratogens from affecting unborn children as well as the rest of the population. Based upon the research to date, phthalates appear to be associated with several developmental systems, including the physiology and function of the reproductive system; hormone levels, obesity, cognitive development; behaviors, including attention deficit hyperactivity disorder and conduct disorder; birth weight, and psychomotor development.

Because of the endemic exposure to phthalates and the presence of the chemicals in the urine and blood of human subjects years after prenatal exposure, continuous monitoring and regulation of phthalates seems essential. As Janssen (2010) stated, it may be necessary to update the 1976 Toxic Substances Control Act and provide government regulatory agencies the authority to take

action in restricting the use of phthalates. The National Academy of Science, the National Toxicology Program, the National Resources Defense Council and other entities have confirmed the research results to alert various government agencies and the general public.

Nowhere in the research did I find any official statements from chemical manufacturer, but I did note that in the EPA's 2012 action plan, the EPA expressed concern about the cost of replacing chemicals in children's products. Walgreen's, S.C. Johnson Company and others have voluntarily changed the exposure to phthalates. Chemical companies may need to voluntarily change their compounds and let the consumer know the contents of the products used on a daily basis. Until significant changes are made in the production and distribution of products of these phthalates, these will continue to affect prenatal development and human development throughout the lifespan.

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