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Review on the Effects of Phthalates on Human Health

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ABSTRACT: A class of commonly used compounds known as phthalates has been shown to be harmful to human health and to be an endocrine disruptor. Phthalates are present in the majority of goods that come into touch with plastics during manufacturing, packaging, or delivery. Even though phthalates have brief half-lives in tissues, long-term exposure to them will negatively affect the endocrine system and the way several organs function. This will have an adverse effect on the reproductive systems of both young children and adolescents as well as the success of pregnancy and the growth and development of the child. In order to lower health hazards, we believe that more nations should impose restrictions or alternative measures for phthalates, even though several have already done so for certain forms of phthalates. The purpose of this page is to list the harmful effects of phthalates on human health, examine the toxicity mechanism, evaluate the dangers, and then offer workable solutions to lower public exposure to phthalates.

KEYWORDS: Endocrine disrupts, plastic, risk assessments, reproductive toxicity, child growth.

I. INTRODUCTION

Since its invention in 1907, plastic has greatly benefited civilization, but it also has several detrimental effects on the environment and human health, which has become a global issue. Humans are continuously exposed to plastics through tainted food, container leachate (such as water bottles and medical devices), urban dust and atmospheric debris that contain microplastics, synthetic clothes, and personal care products (PCPs) like cosmetic packaging. [1] Numerous dangerous compounds would unavoidably leak out after prolonged exposure to plastic. Phthalates, bisphenol A (BPA), and polychlorinated biphenyls (PCB) are the most concerning. Endocrine-disrupting chemicals (EDCs) are compounds that interfere with the normal functions of hormones. Phthalates are a class of chemicals that are mostly added to polyvinyl chloride as plasticizers [2]

PVC plastics to create a softer effect. The endocrine system may be disturbed by phthalates. In recent decades, there have been health concerns about the harmful effects of phthalates on the reproductive system and development. [3] Children are far more susceptible and sensitive to exposure to phthalates than adults are, particularly in the early stages of development. The purpose of this review is to provide an overview of the effects of phthalates on human health, particularly in children, as well as the mechanism and risk assessment of phthalates. It also intends to offer workable solutions to lower public exposure to phthalates [4].

II. BIOMETABOLISM OF PHTHALETES IN HUMAN BODY

Phthalate Metabolism in the Human Body Because phthalates have short biological half-lives (approximately 12 hours), their bio-metabolism in the human body occurs very quickly. Following absorption into cells, hydrolysis is the initial stage of metabolism [9]. The enzyme uridine 50-diphosphoglucuronyl transferase catalyses the second step, conjugation, which creates the hydrophilic glucuronide conjugate [5]. The toxicological fate of phthalates in the body is determined by their kind (Healthcare 2021,9, 603 3 of 9).

While long-branched phthalates primarily undergo a number of bio-transformations, including hydroxylation and oxidation, before being expelled in urine and faeces as phase 2 conjugated compounds, short-branched phthalates are frequently hydrolysed to monoester phthalates and subsequently eliminated in the urine.[6] For instance, the complex branched chains of DEHP may hydrolyze to produce mono(2-ethylhexyl).

Animal studies show that female zebrafish exposed to MEHP have reproductive failure, which may be brought on by changes in endocrine functions (higher cortisol levels). Furthermore, prior research suggested that MCMHP in serum and MECPP in urine could be utilized as appropriate biomarkers based on half-life and distribution pattern. While perspiration can also include certain phthalate molecules (such as DEHP) and their metabolites, the majority of phthalates and their metabolites are found in urine and faeces. Wittassek and Angerer discovered that DEHP's oxidative metabolism varies with age [7]. Younger kids at Mono(2-ethylhexyl) phthalate (MEHP), mono(2-ethyl-5-hydroxyhexyl) phthalate, mono(2-ethyl-5-oxohexyl) phthalate, mono(2-ethyl-5-carboxypentyl) phthalate (MECPP), mono(2-carboxymethylhexyl) phthalate (MCMHP), and other metabolites.[8]

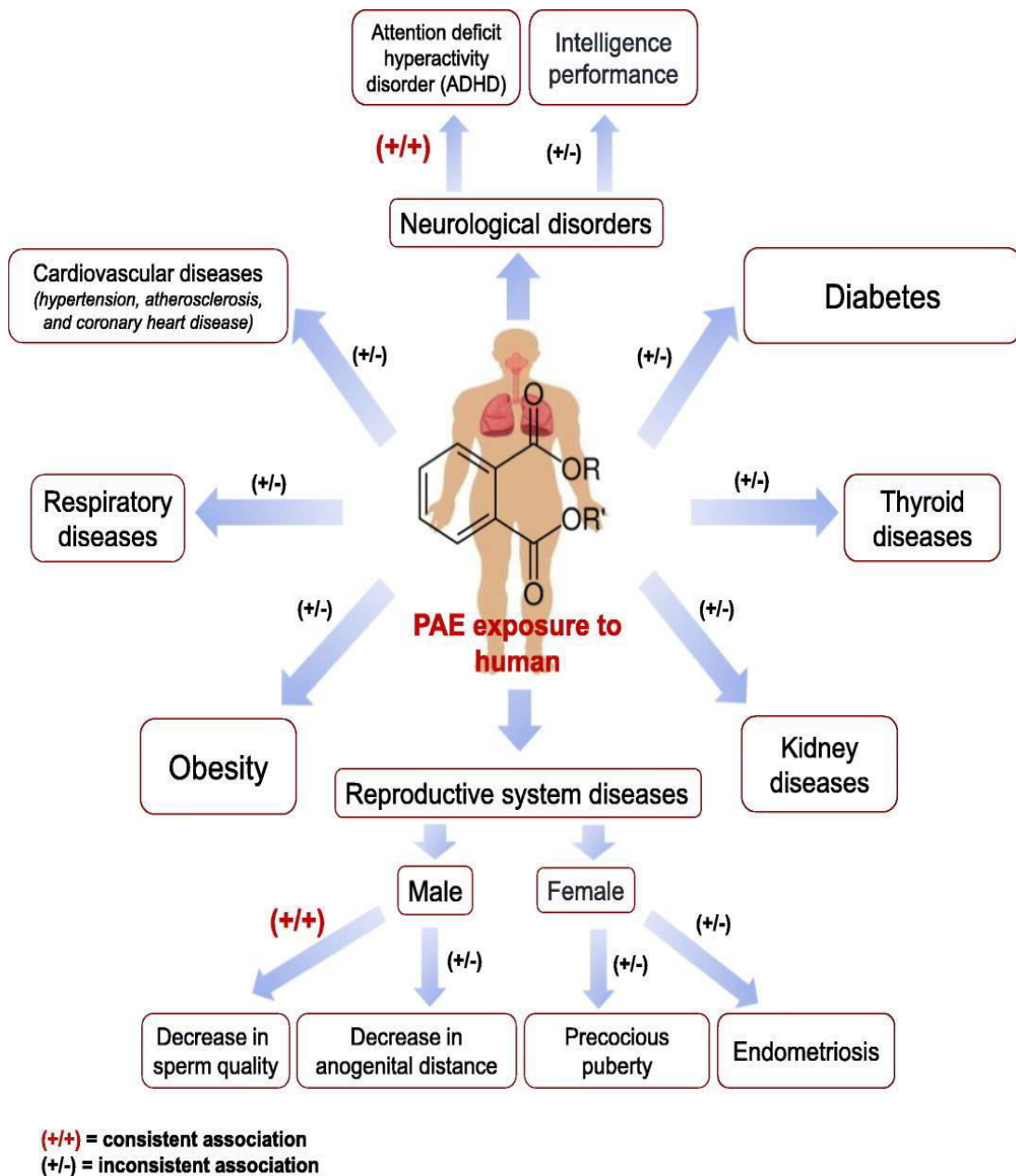


Figure 1

III. IMPACT OF PHTHALATES IN CHILDREN

Epidemiological research on the effects of phthalates toxicity on children concentrated on thyroid function, respiratory symptoms, neurodevelopment, precocious puberty, genital development, and pregnancy outcomes. The effects on children's health are summarized in Anogenital distance, thyroid function, and levels of reproductive hormones (luteinizing hormone, free testosterone, and sex hormone-binding globulin) were all found to be negatively impacted by phthalate exposure in epidemiological investigations.[9] Thyroid cancer has been linked to altered thyroid function. According to a recent Chinese study, exposure to phthalates is linked to altered arginine and proline metabolism, which causes school-age children to become overweight or obese. According 20-year birth cohort study, exposure to phthalates during pregnancy is adversely positively correlated with height in childhood and with both height and weight in infancy . DiDP is linked to the health of the respiratory system in boys younger than five years old, according to another prospective study.[10]

Like BPA, phthalates have also been connected to children's social impairment. According to earlier research, infants and toddlers may be exposed to 5–44 μ g/kg bodyweight/day of DiNP when they come into touch with polymer toys [11]. Approximately 20% of children were exposed to greater amounts of phthalates than the cumulative TDI for DEHP and DBP, according to later research. Nearly all women and children have DBP metabolites, and more than half of phthalate tests conducted on adults older than six years showed positive results for DEHP between 2013 and 2014.[12]

In Australia, TDI-based HI exceedances for adults were uncommon, but TDI values of phthalates were rarely exceeded in children. According to a study that measured the levels of phthalates in Californian air and dust, 8–11% of infants under the age of two years old who were exposed to DEHP exceeded cancer criteria, while 82–89% of toddlers had DBP exposure above reproductive health benchmarks.[14] According to a Chinese study, preschoolers aged three to six years had a larger cumulative risk due to phthalate exposure than those in Germany and Denmark.[13] The primary ingredients are rice, veggies, and flour China is the primary source of DEHP. According to Xu et al., phthalates, primarily DEHP, DnBP, and DiBP, are found in widely used plastic express packing bags, which may be the population's primary source of phthalate exposure at the moment. Furthermore, children were exposed to nearly three times as much DEHP and DnBP as adults when they consumed vegetables cultivated in plastic greenhouses. Phthalates from the packaging are more likely to be absorbed by foods that contain fat, such as dairy and meat [15]. Based on the literature study of healthcare 2021,9, 603 5 of9, we think that the exposure pathway is dependent on the phthalate-containing foods, air, or products.

IV. PHTHALATES TOXICOLOGY AND RISK ASSESSMENT

Phthalates have a median fatal dose (LD50) of 1–30 g/kg bodyweight, and its toxicity is primarily concentrated in the testis, liver, kidney, and thyroid gland tissue, according to animal studies. There is abundant evidence of negative impacts on human and animal development and reproduction. Exposure to DBP at 100 mg/kg bodyweight/day is harmful to foetal development, according to a laboratory experiment conducted on pregnant animals. DEHP has a tolerance daily intake (TDI) of 48 μ g/kg bodyweight and a no-observed-adverse-effect limit of 4.8 mg/kg bodyweight/day. [16] Research revealed that DEP and other low molecular phthalates. Phthalates have a median fatal dose (LD50) of 1–30 g/kg bodyweight, and its toxicity is primarily concentrated in the testis, liver, kidney, and thyroid gland tissue, according to animal studies. There is abundant evidence of negative impacts on human and animal development and reproduction. Exposure to DBP at 100 mg/kg bodyweight/day is harmful to foetal development, according to a laboratory experiment conducted on pregnant animals.[17].Low molecular phthalates, like DEP, have been shown in studies to cause acute irritation of the skin, conjunctiva, and mucous membranes of the nasal and oral canals Exposure to Phthalate is linked to detrimental developmental effects in rats, including decreased growth and birth weight, increased perinatal mortality, and skeletal, visceral, and external abnormalities . The neurological system is relatively vulnerable to modest dosages of DEHP exposure during puberty, according to experiments conducted on male rats [18].

Phthalates have a variety of effects on humans, ranging from altered gene expression to physiological alterations. High molecular weight phthalates have been found to change the methylation status of imprinted genes, which may directly affect protein secretion, the oestrogen response, and the androgen response [19].

V. EPIDEMIOLOGICAL STUDIES ON PHTHALATES

A review and summary of three cross-sectional epidemiological investigations. One study computed internal exposures by combining information on concentrations in different food categories with exposure scenario assumptions, whereas two investigations evaluated exposure using urine phthalate metabolite measurements.[20] Among 1,183 Swiss-German people in Switzerland (mean age = 52.8 years), a cross-sectional study revealed that those who took the predetermined "Fatty presents.

In a related cross-sectional investigation, Trasande and colleagues evaluated the association between log-transformed urine phthalate metabolites and food and caloric consumption (measured by 24-hour dietary recalls) in 2,743 children and adolescents (ages 6–19) from NHANES 2003–2008. Overall, investigations showed that greater levels of high-molecular weight metabolites and sum DEHP metabolites were linked to higher consumption of discretionary solid fat, meats, and calories intake.[21] whereas vegetable eating was linked to increases in low-molecular weight metabolite levels. Per unit meal of meat, poultry, and fish, we found that the levels of high molecular weight phthalates increased by 0.09%, DEHP metabolites increased by 0.02%, MEHP increased by 0.11%, MEHHP increased by 0.10%, and MEOHP increased by 0.10%. In other models, there was a 0.23% increase in DEHP metabolites and a 0.19% increase in high molecular weight phthalates for every additional gram of poultry consumed [18].

VI. INTERVENTION STUDIES

Three strategies designed to lower exposure to dietary phthalates. In a five-day Buddhist Temple Stay program in Korea, Ji and colleagues conducted a quasi-experimental pilot intervention of a strict vegetarian diet on urine phthalate metabolite concentrations in 25 participants. [22] In order to determine the participants' regular intake of beef, hog, chicken, dairy, sheep, goat, duck, turkey, and shellfish (measured in servings/day), a 48-hour diet recall survey was given to them prior to their temple visit. Two of the secondary metabolites of DEHP, 5-oxo-MEHP ($r = 0.33$; $p < 0.05$) and 5-OH-MEHP ($r = 0.31$; $p < 0.05$), showed a substantial and favorable correlation with dairy consumption. Additionally, following the Temple Stay program, both men and women's levels of MEP, MnBP, MiBP, and 5-OH-MEHP considerably dropped, while only females showed a significant decrease in 5-oxo-MEHP. The authors came to the conclusion that dietary changes could considerably lower dietary exposure to phthalates, especially in the short term.[23]

Twenty individuals from the San Francisco Bay region participated in an intervention study that sought to assess the role of food packaging in phthalate exposure by providing them with a catered diet of fresh, primarily organic foods made without the use of plastics. Plastics were not used in the preparation, cooking, or serving of the meals [24].

There were no discernible changes in MEP, MBP, or MBzP metabolites, but the intervention was shown to decrease geometric mean concentrations of MEHP by 53%, MEOHP by 55%, and MEHHP by 56%. Participants' geometric mean concentrations of DEHP metabolites rose at follow-up time periods following the intervention, but the findings were not statistically significant.[8] According to the authors, meals prepared outside the home, canned foods, canned soda, frozen dinners, drinking from polycarbonate water bottles, and microwaving in plastic were all possible exposure sources, based on participant diaries of foods consumed before and after the intervention. However, other significant sources might have been overlooked because diaries were not exhaustive [25].

VII. APPLICATIONS

The plastics industry primarily uses phthalates, including diethylhexyl phthalate (DEHP), dibutyl phthalate (DBP), diethyl phthalate (DEP), di-isononyl phthalate and di-iso-decyl phthalate as plasticizers to create polyvinyl chloride (PVC). Dimethyl phthalate (DMP) and DEP are two examples of short-branched low molecular weight phthalates that are commonly produced and utilized in numerous sectors. [26]

VIII. DISCUSSION

Poultry, various dairy products (such as cream), and fats are frequently contaminated with higher levels of DEHP than other meals, according to the literature assessment. Overall, modest levels of phthalates were discovered in milk, yogurt, eggs, fruits, vegetables, pasta, noodles, rice, drinks, and water. Higher quantities in meals high in lipids were

anticipated given the chemistry of high molecular weight phthalates like DEHP based on usual fat content, there was a notable variation in concentration between dairy products. Compared to yogurt, cream and cheese had higher levels of contamination across all studies among the dairy products tested. The phthalate concentration of poultry was consistently higher than that of other meats, although the contributing variables are unknown [25,26].

These findings because information about the fat content of items was not always provided. Notably, varying quantities of phthalates were found in non-fatty foods including bread and cereal goods.[27]Bread is a major source of DEHP and the largest contributor to overall exposures in the general adolescent and adult population, accounting for 31.4% and 14.06% of exposures, respectively, according to two recent studies carried out in Belgium and Germany. Although it is unclear from these data since information on the fat content of goods was not always supplied, sources of contamination may exist in the grain processing process [28].

IX. FUTURE PROSPECTIVES

The current literature search showed that while there are relatively few data available for Northwest and Southwest China (apart from the Xinjiang Uygur Autonomous Region), a significant number of studies on the presence of PAEs in soils have been carried out in East China [29]. This makes it impossible to get a comprehensive picture of soil PAE contamination across the nation. PAE compounds were extensively found in agricultural and urban soils, as well as in DBP-contaminated areas.[30]

X. CONCLUSION

In conclusion, there is increasing worry about the effects of phthalates on human health, especially given how commonplace they are in consumer goods. Phthalates have been shown to interfere with endocrine function, which may result in problems with metabolism, development, and reproduction. Children and pregnant women are two vulnerable groups that may be especially vulnerable. Even if regulations are changing, more study and greater awareness are necessary to completely comprehend the long-term impacts of phthalate exposure and to encourage safer substitutes in product development. It will be necessary for consumers, legislators, and scientists to work together to protect public health.

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