

EFFECT OF PHTHALATES ON MENTAL HEALTH, REPRODUCTIVE SYSTEM AND ENDOCRINE SYSTEM

Adishri Jain

The Cathedral And John Connon School Mumbai

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ABSTRACT

Phthalates is the common term used to describe a group of chemicals also called plasticisers as they help increase the durability of plastics and don't mix with the chemicals of the plastic. They pollute the surrounding environment by mixing with dust and air.

This article will describe the effects of Phthalates on human life and the reproductive system, on the ecological balance of nature, the mental health and brain function of individuals, and on the endocrine system. We also highlight areas that need more primary research to understand a causal relationship between them, and how this chemical easily gets concealed under other names.

Introduction

Phthalates are man made groups of chemicals or plasticizers and used as common base ingredients in the day-to-day products like cosmetics (personal care products like shampoo, soaps), food items, toys, PVC pipes, hardware materials, packaging equipment, and plastics (Fig. 1). They usually exist in the form of oily, colourless, odourless liquids). They're used as lubricating ingredients in certain cosmetics, and act as fragrance generators. In plastics, toys, and other such appliances, they help by making the material softer and durable Phthalates have multiple varieties and types. For example, DEHP (di-ethylhexyl phthalate), BBP (benzyl-butyl phthalate,) and DINP (diisononyl phthalate), Di-*n*-octylphthalate (DNOP).

Phthalates come under a variety of names, in many personal care products, companies classify phthalates under the term of "fragrance" even though it makes up more than 20 percent of the composition of the product ("Beauty Tip"). This makes it challenging to identify and prevent their usage by consumers. This is especially challenging for children below 3 years of age

because the toys and baby equipment that these kids use, use phthalates as a core building block. For example, companies like Revlon, Calvin Klien, Procter and Gamble.

Unsupervised children are particularly at risk when they put items containing phthalates in their mouths. Phthalates are known to have a positive correlation with obesity, diseases like cancer and multiple other reproductive abnormalities. This data has been collected from a large national sample in the U.S. population. This data is consistent with data from a German biomonitoring study which conducted a similar study and found out the temporal trends over a span of 20 years in a sample of predominantly university students.

Phthalates can enter our body via inhalation, skin absorption, general exposure / presence in air, fragrances we use, and more.

This review aims to see the adverse effects of these phthalates on different processes and systems in our body. It shows the effects of phthalate exposure on our mental health, brain functioning, endocrine system, reproductive system etc. Additionally, it has been observed that DEP, DnBP, BBzP, and DEHP concentrations have declined by approximately 20 to 50 %. Urinary metabolite concentrations of DiBP and DiNP, on the other hand, have increased by over 100%.

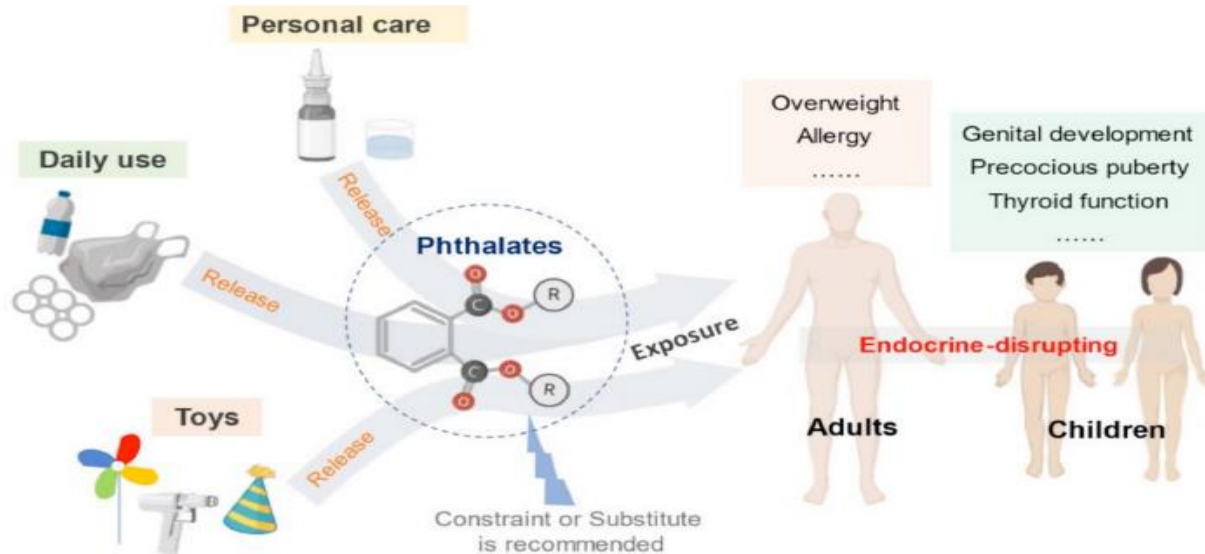


Figure 1 showing the sources and effects that phthalate have on adults and children

Phthalates effects on mental health and brain function

From a young age, motor development and brain development is essential for each child's growth. Multiple researchers have tested out whether the exposure of phthalates has any correlation with mental and behavioural skill development. They concluded that higher exposure

to phthalates led to a late response in motor development. The various different types of phthalates that they tested are monomethyl phthalate, monoethyl phthalate, monobutyl phthalate, monobenzyl phthalate (MBzP), and three di(2-ethylhexyl) phthalate (DEHP) metabolites, namely mono-2-ethylhexyl phthalate (MEHP), mono(2-ethyl-5-hydroxyhexyl) phthalate, and mono(2-ethyl-5-oxohexyl) phthalate.

They manifested lower mental development in girls specifically. Rest of the other three phthalates that they had tested out, had a similar effect when exposed during the prenatal age. They saw a strong correlation in behavioural and mental development and also saw withdrawal symptoms, anxiety and depression in those kids (Table 1.). The study concluded that phthalates can have negative effects on the mental well being, right from the prenatal age. This exposure is detrimental for kids, as seen in Polanska et al. research. The motor development of these 2 year olds' was hampered and their cognition at the age of 7 was lesser than that of other kids who weren't as exposed to phthalates and chemicals as them.

Phthalates have also been seen to lower the production of testosterone. This has been correlated with reduced brain development too.

Table 1: Anxious-shy behaviours were associated with prenatal exposure to MBzP and MiBP

	Prenatal exposure MBzP/MnBP	Prenatal exposure MiBP
Among girls	MBzP: MR=1.15, 95%CI 1.01 to 1.30	-
Among boys	MBzP: MR=1.20, 95%CI 1.05 to 1.36	MR = 1.22, 95%CI 1.02 to 1.47
Both boys and girls	MnBP: MR=1.28 95%CI 1.02 to 1.59	MR = 0.83, 95%CI 0.71 to 0.98

Phthalates' effect on reproduction

Correlation with sudden loss of pregnancy

Zhang et. al. found that pregnancy loss was associated with higher levels of monobutyl phthalate in urine samples. The researchers compared various databases like PubMed, EMBASE, Web of Science and major Chinese literature and came to the same conclusion that they had derived from their research.

Harvard T.H. Chan School of Public Health has also conducted research on a group of women, who were going through a medically assisted reproduction, to show that these hormone-disrupting chemicals like phthalates have an adverse effect on pregnancy. They reached this conclusion after conducting multiple experiments. The results may increase the chances of miscarriage, risk factors for gestational diabetes. The results showed that the women were 60% more likely to lose their pregnancy due to the high concentrations of phthalate than without it. Gestational diabetes may increase the risks of preterm birth and other birth complications. Excessive weight gain during pregnancy might be a factor for gestational diabetes.

Risk of miscarriage

One study showed a statistically significant association between MEHP phthalate exposure and pregnancy loss. A sub analyses found that higher MEHP (strongly associated with inhibition of brain exposure led to a higher chance of an early pregnancy loss. It is also believed that a strong exposure of MEHP at an early age, can increase the chances of pregnancy loss. Phthalates are also known to have an effect on the health of ovaries. With continuous exposure to it, the chances of menstrual irregularities, reduced fertility and slower ovarian function. Another study showed that women who were exposed to a specific type of phthalate DEHP by consumption or utilisation of cosmetic products were 60% more likely to get a miscarriage or pregnancy loss than those who were not.

Phthalates correlation with obesity and weight gain

Endocrine disrupting chemicals interfere with the functioning of hormones and might even be the factors causing weight gain and obesity (Fig. 2). These are referred to as "obesogens".

Obesogens are chemical compounds which can disrupt our metabolism rate, thus promoting fat storage and causing obesity in several ways. It can also lead to diabetes or increase in body fat mass. They might also increase the appetite of an individual. In many cases phthalates have been described as obesogens. In another study there is evidence showing positive correlation between increased obesogen levels, with exposure to phthalates, and body weight or body mass index (BMI) increase in children and adults.

Phthalates effect on reproduction in men

With more exposure to phthalates, greater chances of adverse effects on the male reproductive system has been observed. It has been observed in multiple studies that phthalates exposure has seen a correlation with sperm size decreasing, decreasing sperm count, worsened semen quality, higher chances of developing testicular cancer, greater chances of seeing abnormalities in shape and size of sperm. That being said, out of 12 studies conducted, an inverse relationship was

found between DEP (type of phthalate) exposure and male reproductive health in only 4 studies. No association was observed in the other studies. Therefore, given the lack of multiple studies, we can't fully confirm this correlation.

Sensence happening earlier due to phthalates exposure (Early ageing)

Sensence is the term given to the process of cell division stopping at an early age. They enter the state of permanent growth arrest, which is normal in ageing. However, when this happens earlier than usual, that's when this can cause problems and abnormalities. There have been studies conducted which have found a mild association between the phthalate exposure and DNA damage and oxidative stress in cells. This might play a role in senescence and act as a factor increasing the chances for early ageing. However, not many studies have been conducted in this field and hence we can't come to the conclusion that there is a strong correlation between them. Nevertheless, we can come to this conclusion that chemicals and plasticizers, to some extent, do play a role in the ageing of humans.

Phthalates correlation with hormones during pregnancy

Phthalate exposure during pregnancy and its correlation with sex steroid hormone concentration, is a topic which has seen mixed results. In some instances, the results are not statistically significant, while in others it is. A study done on 1179 children in the US, between the ages of 6 - 19 was conducted where it showed that phthalate exposure affected the prepubertal individuals less than the pubertal ones. This could allude to the fact that phthalate exposure has a positive correlation with sex steroids. Along with implications on sex steroids, implications on foetal development and related health issues have also been seen.

Certain studies have found that with an increase in the concentration of phthalates (DEHP), reduced levels of progesterone have been observed and in turn toxicity in the female reproductive system.

Additionally, a reduction in luteinizing hormone has been observed too. These hormones are crucial for a healthy pregnancy because they help in ovulation and secretion of other essential hormones. As a side effect of these deficiencies, birth abnormalities have also been seen.

During pregnancy, reduction in testosterone concentration is observed with exposure to phthalates, during the gestation period of women. If the child is a boy, there are higher chances that the baby will grow to have reduced testosterone levels. In Sheela et al's study, this has been observed and a correlation has been established between prenatal testosterone concentrations and different phthalates like DEHP, MBP, MEP.

DEHP and MEHP also affect the male reproductive system, leading to male infertility.

This information is crucial for us to better understand the development of maternal and infant health because testosterone has a significant involvement in it. It'll help us understand Phthalates' effects on cardiovascular diseases, hormone mediated reproductive diseases, neurodevelopmental outcomes, and foetal genital tract development.

These results, however, need more experiments to be conducted for substantial evidence to be gathered to prove this theory.

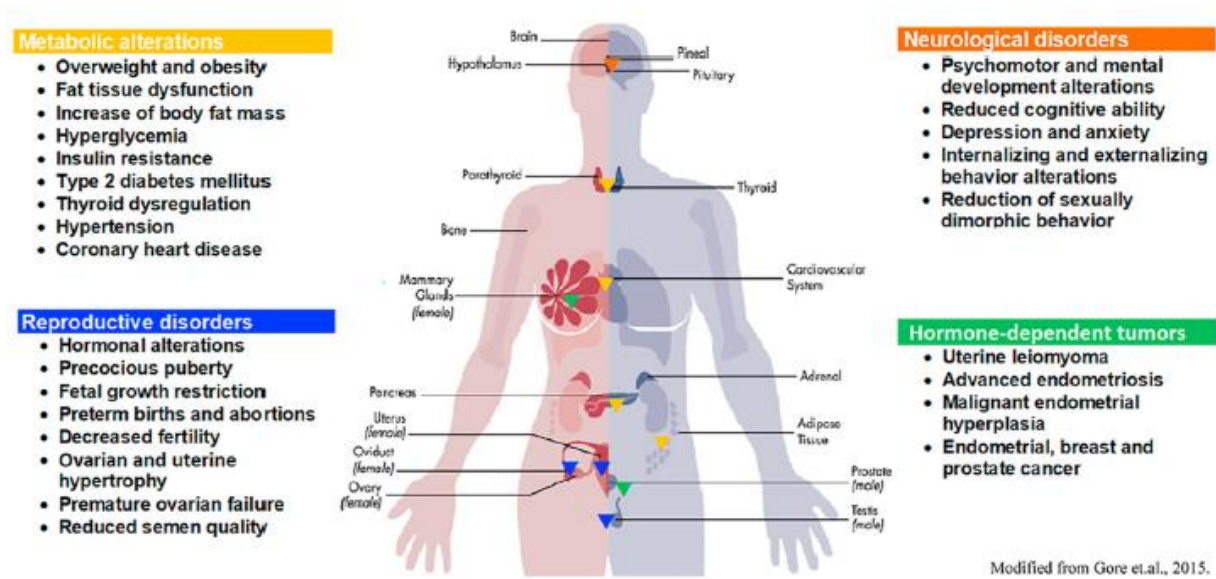


Figure 2: Detailed impacts of phthalate exposure

Phthalates effect on hormones and the endocrine system

Placental corticotropin releasing hormone

This hormone is important during pregnancy to allow foetal maturation and regulation of time of delivery. It also helps increase maternal serum cortisol levels during the third trimester.

Phthalates may disrupt maternal-foetal-placental endocrine pathways. They do so by mimicking or blocking the pathways. Especially the androgen and oestrogen receptors. This can have a negative effect on the pregnancy outcomes and overall development of the child. Placental corticotropin releasing hormone (pCRH) is critical for healthy pregnancy and child development, but understudied as a target of endocrine disruption. More primary research in this area can bring about more constructive information and corrective substitutes.

Hypothalamic pituitary Gonadal axis

The Hypothalamic Pituitary Gonadal Axis, also called the HPG, is the term given to the Hypothalamus and the pituitary gland gonadal glands, together. This axis is responsible for regulating reproduction and development. As mentioned earlier, phthalates can reduce the amount of testosterone production, reduce the sperm count and cause other such reproductive issues. The HPG is what gets adversely affected and hence causes these changes. More research needs to be done to establish a stronger control between the two though.

Discussion

This analysis supports the theory that phthalates have significant detrimental effects on the human body. When exposed in excess quantities, these chemicals have an adverse effect on multiple body systems. They can lead to higher chances of delayed mental growth and anxiety. Exposure to phthalates can increase chances pregnancy Exposure to certain chemicals can disrupt the hormonal balance necessary for a safe pregnancy, potentially affecting the course of pregnancy itself. Phthalates can affect prenatal babies, young infants, adolescents and adults too. Since phthalates are used universally, it is essentially that consumers have an easier way to identifying them in the products they purchase.

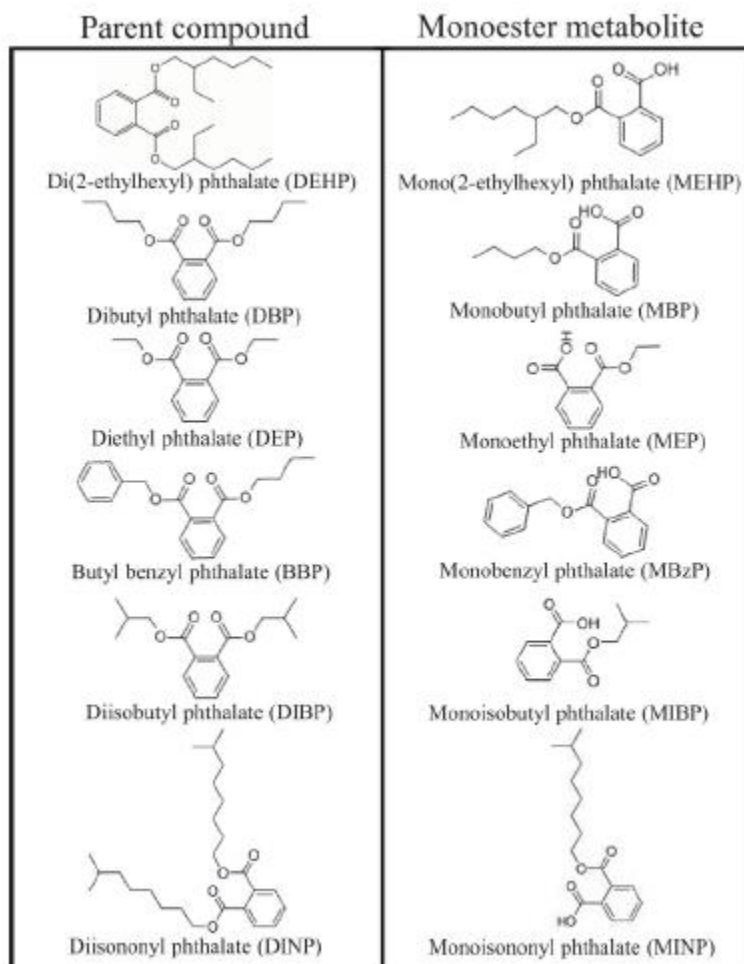
Phthalates are present in various consumables in high concentrations. As discussed here, they can have a detrimental effects on us. The reproductive system faces major issues such as miscarriage, pregnancy loss, and more. Phthalates affect the production and secretion of our Phthalates make living safe and healthy challenging for all unwittingly consuming them. In 2017, the Consumer Product Safety Commission banned the consumption of 8 types of phthalates present in children's toys.

The issue of over consumption of phthalates is a serious issue which if not attended to, is likely to cause many more deaths indirectly. Unfortunately, there is not much awareness about this topic for the general public. More studies on the side effects of these chemicals should be carried out. Awareness should be raised via public health advisories. As more chemical classes beyond phthalates are identified, it is likely that people become more aware and research ways to substitute toxic chemicals.. In the present, it is challenging to find a chemical which has the exact same function as phthalates but does not adversely affect the human body. We can opt for natural substances like coconut oil, jojoba oil, etc in cosmetics and choose biodegradable plastics to avoid the chances of coming in contact with phthalates.

In the future, if we don't stop consuming phthalates, there are high chances of adopting problems it brings along, that we can't even imagine.

This research is an important upcoming field and needs a lot more primary research to help find organic substitutes of Phthalates so that the use of this chemical is permanently eradicated and human health is retained naturally.

Table 2: showing chemical structures of common phthalates and their monoester metabolites



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