ABSTRACT
Our literature review study reflects the light on some chemical substances which are widely used in many & different aspects of our children daily practices & try to get the answers for the following important questions. Do these chemicals that our children are widely exposed to since even their prenatal period & throughout their lives have real high risks & dangers on their health? Is the use of these chemicals essential for our kids or we can avoid and replace them with other non-risky substances & hazardous chemical free products ...!? Recently, a lot of systematic review studies have been done to investigate the possible relations between the most common chemical substances that we use daily and possible risks & health problems that may affect our children. Among the chemicals that have been studied intensively in the last few years are Phthalates which are known as endocrine disruptors due to their anti-androgenic and/ or estrogenic effects!

The purpose & Objectives of our study are to provide an overview of some widely and commonly used chemicals that are introduced to many of the products essentially used by our children daily, and the possible relations between their use and some of the common health problems & disorders that affect children in order to raise the awareness among parents & health care providers regarding their potential health impacts on children and to provide a proper guidance that help to minimize the avoidable exposure to these risky chemicals and replace them with hazardous chemicals free products till we get enough studies that prove or disprove their risks & effects.

Methods & Results: Our study tries to search through, emphasis on & spot the light on the use of common chemical substances (Phthalates) that are widely used in most of our children life aspects, searches for their possible risks & hazards on our kids’ health, tries to get relations & connections between these substances & common pediatric health problems & disorders. In our study we reviewed the data collected from many evidences based systematic reviews and Cohort studies have dealt with these hazardous substances & stated the high incidence of their risks & their bad impacts on our kids’ health & prove the relation of these chemicals to certain respiratory problems specially wheezing in childhood, ADHD, some atopic conditions and endocrine disruptions among children.

Recommendations: Our study concluded & suggested that it is better to eliminate exposure to these chemicals as evidences are rising against their safety. It’s very important to increase the awareness among parents & health care providers regarding the possible risks of these chemicals and provide them the most proven practical tips for their avoidance. Further epidemiological studies should be conducted in the future to enhance our knowledge in this area.

Phthalates Our Hidden Enemy, Our Threatened Future
Objective: • What is phthalate?
• How are we exposed to?
• Phthalates in human biomonitoring.!!
• Phthalate effects on children …
• How to avoid its exposure?

Introduction
• We live in a world of chemicals.
• Chemicals make our life easier, more convenient and more comfortable, but is it healthier?
• Since 1970’s, more than 85000 chemicals have been approved for commercial use, yet only just one thousand of them have been examined and graded for their harmful potential.
• Most chemicals are used before being tested for safety and would only be regulated or banned after showing harmful effects on human, making us unwillingly experimental mices in this industrial world.

When we talk about chemicals, we don’t only mean the pollution resulted from industry.
we talk about things that we buy everyday presuming that if something is sold in supermarkets or pharmacies, and if everyone consume, then they should be safe. But the truth is bitter.

So… What is phthalates?
• Phthalates are a group of man-made chemicals, added to poly-vinyl chloride (PCV) to make this brittle plastic more flexible and durable (plasticizers).
• They were invented in 1920s and since then we witnessed a burst in plastic use globally, making us the third or fourth generation to be exposed to these chemicals.
• Many different phthalates exist with different properties, uses, and health effects.
• High-molecular weight phthalates (e.g. di-2-ethylhexyl) phthalate (DEHP) are primarily used as plasticizers in the manufacture of flexible vinyl plastic which, in turn, is used in:
  • ** Waterproofs, raincoats & flip flop Clothes …!!
  • Domestic & construction: Flooring, Wall Coverings, Shower Curtains and Hosepipes
  • Food contact applications like containers, food packaging and wraps ..!
  • Toys, school supplies and childcare articles.
  • Medical devices, like blood bags and tubing.

PVC products may contain up to 50% (by weight) phthalates, and the more flexible the product is the more phthalate it contains..!
• Low-molecular weight phthalates are used as solvents in personal-care products to hold fragrance and make products more effectively penetrate and moisturize the skin e.g. in Perfumes, Lotions, Cosmetics, Shampoos, After-shave, Nail polishes, Air fresheners.
and in lacquers, varnishes and coatings, including those used to provide timed releases in some pharmaceuticals.

How are we exposed to phthalates?
Since phthalates are not chemically bound to PCV polymers, they can leach, migrate or evaporate into indoor air, dust, food stuff and other materials.

Human exposure to phthalates occurs through inhalation or ingestion of contaminated air and food as well as skin contact.

Phthalates in processed and packaged food
• Processed and packaged food are the main source of human exposure.
  • mostly in fatty food, dairy products, processed cheese, processed meat, fish and oil, grain, ultra-processed food like soft drinks and fruit drinks, ready-to-eat-food and even in baby food and formulas.
  • This contamination could happen either during processing or leaching from the packaging before consumer use.
  • Phthalates exposures have also been associated with food venues, including fast food restaurants, school cafeteria lunches and dining out.

Daycare products and cosmetics
• Phthalates have proven to be very effective softeners in daycare products like hair conditioners, hairsprays and body lotions so the use of certain personal care products especially makeup, lotion, emollients and sunscreens is associated with higher exposure to phthalates.
• Studies show that phthalates exist in the products when manufactured and their concentrations increase with the storage time indicating the possibility of leaching and migration of phthalates from the container also into the product.
• Phthalates made big news in 2008 when the American Academy of Pediatrics reported that infants exposed to infant-care products, specifically baby shampoos, baby lotions, and baby powder, showed higher than normal levels of phthalates in their urine …!!
• This is also important in adolescent girls because they are in a critical age in hormonal development and have high use of personal care products.

Toys and childcare articles made from PVC
• Plastic toys and childcare articles made from PVC are a great source of children exposure to phthalates as they can leach and contaminate the presumed safe surrounding environment or due to the hand-mouth habit in younger children.
• Soft toys contain higher levels of phthalates as compared to hard toys as primary function of phthalates is softening of hard plastic material.
• Because of their potential effects on human health, the European Union has banned the use of six specific phthalates in products for children.
• Toys and childcare articles made of PVC in other countries still contain variable levels of phthalates exceeding the EU regulations sometimes highly …!!
• If a toy is not designed to be sold on the European market by the manufacturer, it seems to be more likely to contain a Phthalic acid ester.

Phthalates in dust and indoor air
• Those dust particles accumulating on our floors might seem like a minor annoyance, but they could be exposing us to potentially harmful chemicals including phthalates.
• Studies confirm the occurrence of multiple phthalates sometimes in high concentrations in indoor dust, with DEHP being the most frequently detected phthalates in indoor dust.
• Humans are exposed to phthalates in dust via ingestion, inhalation and dermal uptake. Children are known to be more exposed to dust than adults due to their proximity to the floor and frequent hand-to-mouth behavior.
• The age of the building, presence of foam mattresses and PVC flooring, presence of old soft plastic toys and the amount of plastic toys, the presence of electronic devices and the low cleaning frequency were associated with higher levels of phthalates in indoor dust

Iatrogenic phthalate exposure
• Flexible plastic devices in hospitals like blood products bags, intravenous tubing, endotracheal tubes, feeding tubes, catheters and cannulas and others are most commonly made of polyvinyl chloride (PVC).
• In November of 2014, Scientists at Johns Hopkins Bloomberg School of Health reported that.. “Because of phthalates in medical devices, premature babies admitted to the NICU can be exposed to 4,000 to 160,000 times the amount of phthalates considered safe”..!
Phthalates in medication
• A lesser-known potential source of exposure is the timed-release coatings on certain pharmaceuticals and dietary supplements.
• Phthalates are used also as excipients in numerous RX and OTC drug products and supplements from a wide range of therapeutic categories.
• Up to 50-fold higher levels of urinary phthalate metabolites have been observed in users of phthalate-containing drug products compared with non-users..!
• Studies in children are lacking..!

Phthalates exposure
• Phthalates are rapidly metabolized and excreted in urine as a major elimination pathway, so the measurement of phthalate metabolites in urine is used to detect the recent exposure.
• Yet Phthalate metabolites have been measured in various other body fluids, serum, semen, breast milk, and saliva.
• Phthalates can cross the placental barrier and have been measured in amniotic fluid in human studies.
• The estimated daily exposure to one major phthalate, di(2-ethylhexyl) phthalate (DEHP), ranges from 3–30 μg/kg/d.
• According to the Forth National Report on Human Exposure to Environmental Chemicals, nearly all Americans in every age group (age 6 or older) have detectable levels of phthalate metabolites and other endocrine disrupting chemicals in their urine.
• In Europe, according to the DEMOCOPHES project phthalate metabolites were detected in almost all participants (1844 mother-child pairs) ..!
• In general, DEMOCOPHES results show that younger children (6-8 years) have higher exposure levels compared to older children (9-11 years), and higher levels in children compared to mothers, with the exception of MEP which is not regulated and is mainly used in cosmetics.
• A possible explanation is children’s relatively higher intake: they are more exposed to dust, playing nearer the ground, and have more frequent hand-to-mouth contact; and they eat more than adults in relation to their weight.
• Consumption of convenience food, use of personal care products and indoor exposure to vinyl floors and wallpaper have all been linked to higher phthalate levels in urine.
• In Australia, data suggest that phthalate metabolites concentrations are at least two times higher than in the United States and Europe ..!
• A study in Saudi Arabia in 2017 measured major phthalate metabolites in urine samples of children aged 3-9 years…;

"The results showed that urinary levels of some phthalates were detected at higher levels than those reported previously in children worldwide, that was mostly related to the frequency of eating out, consumption of hamburgers, canned food, ice cream, and the use of sun creams or sun spray”.

Why phthalates raised concern ?
• Phthalates have received considerable attention because of their ubiquitous presence in the environment, frequent detection in human biomonitoring studies, and demonstrated toxicity in rodents and humans.
• Phthalates are approved to have estrogenic effect making them endocrine-disrupting chemicals (EDCs).

Phthalates and reproductive system
• Exposure to phthalates is of great concern, as they have been suspected to have anti-androgenic and estrogenic effects, which may alter the reproductive development of children.
• Animal studies indicate that gestational phthalate exposure is associated with adverse health outcomes, including disruption of endocrine and reproductive function and development.
• In females it induces pathological changes in ovaries, affects organ weights, disrupts estrous cyclicity, reduces fertility-related indices, and causes some breeding complications.
• While in males, animal studies provide consistent evidence that certain phthalates target the developing reproductive system causing any genital anomaly. The connection is so clear the disorder is termed Phthalate Syndrome (PS) and the effects mirror a set of reproductive symptoms seen in human males, termed Testicular Dysgenesis Syndrome (TDS).
• In human .., increased evidence shows that phthalates have adverse effects on Leydig cell development, thus causing lower androgen and Insulin-like 3 production and increasing the odds of any male newborn genital anomaly (termed Testicular Dysgenesis Syndrome (TDS) including cryptorchidism, hypospadias, shortened anogenital distance and isolated hydrocele.
• It also leads to disrupted gonadal function and spermatogenesis (low sperm counts and sperm motility and maturation).
• It alters reproductive function of adolescent men including total testicular volume, reproductive hormones and semen volume.

Phthalates and neurodevelopment
• We are witnessing an alarming increase in learning and behavioral problems in children.
• Although most of these problems are multifactorial, there are increased evidences that exposure to phthalate either prenatally or after birth can affect different aspects of neurodevelopment in children.
• It is strongly suggested to increase the odds of ADHD, attention deficit disorder, learning disability, and social, thought, attention, cognitive and behavioral problems and may also affect the language development in children.
• The strongest evidence is for motor effects and BBP exposure in girls.

Phthalates have also been associated the development of ;
• overweight and obesity in school-age children.
• Increased BMI and waist circumference in adults and children.
• Increased insulin resistance, a precursor to diabetes, in teenagers
• Childhood asthma.
• May worsen pulmonary function and airway inflammation in asthmatic children.

How to avoid phthalate exposure
• We simply cannot escape our exposure to man-made chemicals, but there is a lot we can do to moderate & control our exposures.
• While onetime exposure to chemicals is often considered “safe”, many of these products are used every day, and the effects of long-term exposure, especially when combined with other chemicals, is largely unstudied and unknown.

Awareness;
Given the lax regulation of chemicals and the reactionary approach of governments’ regulators, it is up to the consumer to be diligent about reading labels and making healthy choices to limit exposure to chemicals and toxins.
It is ideal to adopt the Precautionary Principle: “until a chemical is found to be harmless, try to not use it”. The precautionary principle means that you are maintaining awareness of what you are putting on and in your body and taking steps to avoid exposing yourself unnecessarily to toxins in your household and environment.

Minimize plastic use;
- Limit exposure to plastics, especially anything with the number 3 or 7 on them.
- Use glass, ceramic, or metal containers for food and drink.
- If you have to use plastic, don’t microwave it, or wash it in the dishwasher to limit the leaching out of chemicals.
- Minimize plastic toys especially soft ones, instead you can use wooden toys or stuffed ones. Also, consider using silicone bottle nipples and teethers, and consider glass bottles for infants and babies that cannot feed themselves yet.

Avoid food with high concentration of phthalates;
- Avoid packaged foods: Studies have also shown that phthalates are particularly high in some packaged foods. Try to avoid these foods, especially for children.
- Foods that are higher in fat -- meats and cheeses, for instance -- are particularly prone to chemical leaching.
- Dairy items like heavy cream, ice cream and cheese had high to very high levels of phthalates.

Stay away from fragrance;
- Unfortunately, you will very rarely see phthalates listed on a product label. Luckily, there are clues. When it comes to cosmetics, the word “fragrance” or “perfume” on a label almost always means phthalates. What you want to see are claims like: “no synthetic fragrance” or “scented with only essential oils” or “phthalate-free.” And always use only natural air freshener.
- Avoid personal care items where the scent is strong and lasts longer than 15-30 minutes as these products likely contain synthetic chemicals instead of pure essential oils.
- Minimize the use of unnecessary personal care products (The average man uses five to seven personal care products a day. The average woman uses nine to twelve products. The average teenage girl uses seventeen) and you can follow the rule (the less ingredients is better).
- Good resources for more information on the topic and safer alternatives include websites like EWG (ewg.org), Breast Cancer Prevention Partners (bcpp.org), IARC (iarc.fr or monographs.iarc.fr), National Institute of Environmental Health Sciences (niehs.nih.gov), National Cancer Institute (cancer.gov), and the American Cancer Society (cancer.org).

References:
- A Review of Biomonitoring of Phthalate Exposures.2019
- Phthalates and other additives in plastics: human exposure and associated health outcomes 2009.
- Population Exposure to Phthalate-containing Drugs. 2017
- Intake estimates of phthalate esters for South Delhi population based on exposure media assessment 2014.
- Concentrations of phthalates and bisphenol A in Norwegian foods and beverages and estimated dietary exposure in adults.2014.
- Determination of contamination pathways of phthalates in food products sold on the Belgian market.2014
- Persistent plasticizers and bisphenol in the cheese of Tunisian markets induced biochemical and histopathological alterations in male BALB/c mice 2018.
- Termination of phthalate diesters and monoesters in human milk and infant formula by fat extraction, size-exclusion chromatography clean-up and gas chromatography-mass spectrometry detection 2016.
- Variability and predictors of urinary concentrations of phthalate metabolites during early childhood 2014 Recent fast food consumption and bisphenol A and phthalates exposures among the U.S. Population in NHANES, 2003–20102016
- Dietary sources of cumulative phthalates exposure among the U.S. general population in NHANES 2005–2014, 2018
- Endocrine society/Phthalates, found in hundreds of household products, may disrupt sex development of male fetus
- Analysis of phthalate esters in two different baby care products available in United Arab Emirates 2019.
- Personal care product use as a predictor of urinary concentrations of certain phthalates, parabens, and phenois in the HERMOSA study 2019.
- Children with atopic dermatitis and frequent emollient use have increased urinary levels of low-molecular-weight phthalate metabolites and parabens 2017
- Analysis and Assessment of Exposure to Selected Phthalates Found in Children’s Toys in Christchurch, New Zealand 2018.
- Assessment of toxic metals and phthalates in children’s toys and clays 2013.
- Simultaneous GC-MS determination of eight phthalates in total and migrated portions of plasticized polymeric toys and childcare articles 2015
- Survey on plasticizers currently found in PVC toys on the Swiss market: Banned phthalates are only a minor concern. 2017
- Fate and Transport of Phthalates in Indoor Environments and the Influence of Temperature: A Case Study in a Test House 2015
- Phthalate esters in indoor dust from several regions, China and their implications for human exposure 2019.
- Comparative Assessment of Human Exposure to Phthalate Esters from House Dust in China and the United States 2011.
- Phthalate and non-phthalate plasticizers in indoor dust from childcare facilities, salons, and homes across the USA 2017
- Vinyl flooring in the home is associated with children’s airborne butylbenzyl phthalate and urinary metabolite concentrations.2015
- Exposure to phthalates in house dust and associated allergies in children aged 6-12years 2016.
- Children’s Phthalate Intakes and Resultant Cumulative Exposures Estimated from Urine Compared with Estimates from Dust Ingestion, Inhalation and Dermal Absorption in Their Homes and Daycare Centers 2013.
• Phthalates and critically ill neonates: device-related exposures and non-endocrine toxic risks 2014
• Hidden Toxicity in Neonatal Intensive Care Units: Phthalate Exposure in Very Low Birth Weight Infants 2016
• Population Exposure to Phthalate-containing Drugs 2017, Population Exposure to Phthalate-containing Drugs 2017,
• Identification of phthalates in medications and dietary supplement formulations in the United States and Canada 2012
• Medications as a potential source of exposure to phthalates in the U.S. population 2009
• European Medicines Agency. Guideline on the use of phthalates as excipients in human medicinal products 2012
• Guidance for industry limiting the use of certain phthalates as excipients in CDER-regulated products 2012
• Cumulative exposure to phthalates from phthalate-containing drug products: a Danish population-wide study
• Metabolism of phthalates in humans. 2007
• Serum concentrations of phthalate metabolites are related to abdominal fat distribution two years later in elderly women 2012
• Altered semen quality in relation to urinary concentrations of phthalate monoester and oxidative metabolites. 2006
• Detection of 20 phthalate esters in breast milk by GC-MS/MS using QuEChERS extraction method. 2019,
• Concentrations of phthalate metabolites in breast milk in Korea: estimating exposure to phthalates and potential risks among breast-fed infants 2016,
• Determination of phthalate diesters and monoesters in human milk and infant formula by fat extraction,
• size-exclusion chromatography clean-up and gas chromatography-mass spectrometry detection 2016
• Transplacental transfer of monomethyl phthalate and mono(2-ethylhexyl) phthalate in a human placenta perfusion system 2007,
• Maternal exposure to endocrine disruptors and placental transmission: a pilot study 2018
• Distribution of Phthalate Metabolites between Paired Maternal-Fetal Samples 2018.
• EDC-2: The Endocrine Society’s Second Scientific Statement on Endocrine-Disrupting Chemicals
• Center of Disease Control and Prevention. Forth national report on human exposure to environmental chemicals updated 2017,
• Urinary Phthalate Concentrations in Mothers and Their Children in Ireland: Results of the DEMOCOPHS Human Biomonitoring Study. 2017
• Exposure determinants of phthalates, parabens, bisphenol A and triclosan in Swedish mothers and their children 2014
• Concentrations of phthalates and DINCH metabolites in pooled urine from Queensland, Australia 2016
• Urinary phthalate metabolites among children in Saudi Arabia: Occurrences, risks, and their association with oxidative stress markers 2017
• The estrogenic potential of the phthalate esters 2000, The estrogenic activity of phthalate esters in vitro 1997
• The estrogenic activity of phthalate esters in vitro 1997.
• Components of plastic: experimental studies in animals and relevance for human health 2009.
• Sex Steroid Hormone Levels and Reproductive Development of Eight-Year-Old Children following In Utero and Environmental Exposure to Phthalates 2014
• Prenatal exposure to an environmentally relevant phthalate mixture disrupts reproduction in F1 female mice 2017
• Assessment of phthalates/phthalate alternatives in children’s toys and childcare articles: Review of the report including conclusions and recommendation of the Chronic Hazard
• Advisory Panel of the Consumer Product Safety Commission. 2015
• Genotoxic, histologic, immunohistochemical, morphometric and hormonal effects of di-(2-ethylhexyl)-phthalate (DEHP) on reproductive systems in pre-pubertal male rats 2018
• Consumer Product Safety Commission. Toxicity review for Di-n-butyl phthalate 2017
• Phthalate-Induced Fetal Leydig Cell Dysfunction Mediates Male Reproductive Tract Anomalies 2019
• Consumer Product Safety Commission. Toxicity review for diethyl phthalate 2018,
• Exposure to phthalates and breast cancer risk in northern Mexico. Environ Health Perspect 2010,
• First trimester phthalate exposure and male newborn genital anomalies. 2016,
• Genotoxic, histologic, immunohistochemical, morphometric and hormonal effects of di-(2-ethylhexyl)-phthalate (DEHP) on reproductive systems in pre-pubertal male rats 2018,
• Lifelong exposure to di-(2-ethylhexyl)-phthalate induces tumors in liver and testes of Sprague-Dawley rats 2005
• Phthalate exposure and reproductive parameters in young men from the general Swedish population 2015
• A crossover-cross back prospective study of dibutyl-phthalate exposure from mesalazine medications and semen quality in men with inflammatory bowel disease. 2016
• Phthalate-Induced Fetal Leydig Cell Dysfunction Mediates Male Reproductive Tract Anomalies 2019,
• Amniotic fluid phthalate levels and male fetal gonad function 2015
• Prenatal phthalate exposure and reproductive function in young men 2015
• Phthalate exposure, even below US EPA reference doses, was associated with semen quality and reproductive hormones: Prospective MARHCS study in general population 2017
• Phthalate exposure and semen quality in fertile US men 2016
• Association of urinary phthalate metabolites concentrations with body mass index and waist circumference 2018,
• Urinary phthalates and increased insulin resistance in adolescents 2013
• Phthalate esters and childhood asthma: A systematic review and congener-specific meta-analysis 2017
• Exposure to phthalates aggravates pulmonary function and airway inflammation in asthmatic children 2018
• Environmental exposures and cancer: using the precautionary principle 2019
• Phthalate levels and related factors in children aged 6-12 years 2017
• Obesity or diet? Levels and determinants of phthalate body burden – A case study on Portuguese children 2018,
• Food packaging and bisphenol A and bis(2-ethylhexyl) phthalate exposure: findings from a dietary intervention 2011,
• Dietary phthalate exposure in pregnant women and the impact of consumer practices 2014
• Pharmaceuticals, personal care products and endocrine disrupting agents in the environment—a review. CLEAN–Soil Air Water 2009
• Environmental exposures and cancer: using the precautionary principle 2019,