hero.3466563

Absalan, F; Saremy, S; Mansori, E; Taheri Moghadam, M; Eftekhari Moghadam, AR; Ghanavati, R. (2017). Effects of Mono-(2-Ethylhexyl) Phthalate and Di-(2-Ethylhexyl) Phthalate Administrations on Oocyte Meiotic Maturation, Apoptosis and Gene Quantification in Mouse Model. 18: 503-513.

OBJECTIVE: Phthalates, which are commonly used to render plastics into soft and flexible materials, have also been determined as developmental and reproductive toxicants in human and animals. The purpose of this study was to evaluate the effect of mono-(2- ethylhexyl) phthalate (MEHP) and di-(2-ethylhexyl) phthalate (DEHP) oral administrations on maturation of mouse oocytes, apoptosis and gene transcription levels.

MATERIALS AND METHODS: In this experimental study, immature oocytes recovered from Naval Medical Research Institute (NMRI) mouse strain (6-8 weeks), were divided into seven different experimental and control groups. Control group oocytes were retrieved from mice that received only normal saline. The experimental groups I, II or III oocytes were retrieved from mice treated with 50, 100 or 200 µl DEHP (2.56 µM) solution, respectively. The experimental groups IV, V or VI oocytes were retrieved from mouse exposed to 50, 100 or 200 µl MEHP (2.56 µM) solution, respectively. Fertilization and embryonic development were carried out in OMM and T6 medium. Apoptosis was assessed by annexin V-FITC/Dead Cell Apoptosis Kit, with PI staining. In addition, the mRNA levels of Pou5f1, Ccna1 and Asah1 were examined in oocytes. Finally, mouse embryo at early blastocyst stage was stained with acridine-orange (AO) and ethidium-bromide (EB), in order to access their viability.

RESULTS: The proportion of oocytes that progressed up to metaphase II (MII) and 2-cells embryo formation stage was significantly decreased by exposure to MEHP or DEHP, in a dose-dependent manner. Annexin V and PI positive oocytes showed greater quantity in the treated mice than control. Quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) revealed that expression levels of Pou5f1, Asah1 and Ccna1 were significantly lower in the treated mouse oocytes than control. The total cell count for blastocyst developed from the treated mouse oocytes was lower than the controls.

CONCLUSION: These results indicate that oral administration of MEHP and DEHP could negatively affect mouse oocyte meiotic maturation and development in vivo, suggesting that phthalates could be risk factors for mammalians' reproductive health. Additionally, phthalate-induced changes in Pou5f1, Asah1 and Ccna1 transcription level could explain in part, the reduced developmental ability of mouse-treated oocytes.

hero.3469610

Ahmadivand, S; Farahmand, H; Teimoori-Toolabi, L; Mirvaghefi, A; Eagderi, S; Geerinckx, T; Shokrpoor, S; Rahmati-Holasoo, H. (2016). Boule gene expression underpins the meiotic arrest in spermatogenesis in male rainbow trout (Oncorhynchus mykiss) exposed to DEHP and butachlor. Gen Comp Endocrinol 225: 235-241. http://dx.doi.org/10.1016/j.ygcen.2015.05.011.

Boule, the ancestor of the DAZ (Deleted in AZoospermia) gene family, in most organisms is mainly involved in male meiosis. The present study investigates the effects of the plasticizer DEHP (50mg/kg body weight) and herbicide butachlor (0.39mg/L) on male rainbow trout (Oncorhynchus mykiss) for a 10-day period in two independent experiments. The results showed that plasma testosterone (T) concentrations were significantly lower in fish exposed to either DEHP or butachlor compared to the control fish (P<0.05). Fish showed a significantly elevated hepatosomatic index (HSI) in the butachlor treatment (P<0.05). However, no significant difference was observed in HSI values in the DEHP treatment (P>0.05). In addition, no significant differences were found in the gonadosomatic index (GSI) in both DEHP and butachlor treatments (P>0.05). Histologically, testes of male trout in the control groups were well differentiated and filled with large numbers of cystic structures containing spermatozoa. In contrast, the testes of male trout contained mostly spermatocytes with few spermatozoa in both treated group, suggesting that DEHP and butachlor may inhibit the progression of meiosis. Also, boule gene expression was significantly lower in the testes of male trout affected by DEHP and butachlor in comparison with their control groups (P<0.05), which confirmed the meiotic arrest in affected trout. Based on the results, the present study demonstrated that DEHP and butachlor can inhibit the progression of spermatogenesis in male trout, potentially by causing an arrest of meiosis, maybe due to down-regulation of boule gene expression through T and/or IGF1 via ERK1/2 signaling in T-independent pathways. In addition, these results confirmed that boule can be considered as a predictive marker to assess meiotic efficiency.

hero.3455008

Ait Bamai, Y; Araki, A; Kawai, T; Tsuboi, T; Saito, I; Yoshioka, E; Cong, S; Kishi, R. (2016). Exposure to phthalates in house dust and associated allergies in children aged 6-12years. Environ Int 96: 16-23. http://dx.doi.org/10.1016/j.envint.2016.08.025.

Phthalates are widely used as plasticizers in household products. Several studies have reported an association between phthalate exposure and an increased risk of allergies. The present study estimated phthalate exposure in children aged 6-12years and assessed potential correlations with allergies. House dust samples were collected from floors and multi-surface objects >35cm above the floor. Urine samples were collected from the first morning void of the day. Daily phthalate intake (DIdust and DI) was estimated using both house dust and urinary metabolite concentrations. Exposure to di-2-ethylhexyl phthalate (DEHP) in floor dust was associated with parental-reported rhino-conjunctivitis. After stratification by gender, this trend was found to only occur in boys. Furthermore, urinary mono-isobutyl phthalate was inversely associated with parental-reported wheeze in boys. DIdust of benzyl butyl phthalate (BBzP) and DEHP were significantly correlated with DI_BBzP and DI_DEHP, respectively. These correlations were stronger with floor than with multi-surface dust. Our results suggest that, among Japanese children, house dust from low surfaces, such as living room floors, might play a meaningful role in the indoor environmental exposure pathway for BBzP and DEHP.

hero.3350346

Al Salloum, H; Saunier, J; Tfayli, A; Yagoubi, N. (2016). Studying DEHP migration in plasticized PVC used for blood bags by coupling Raman confocal microscopy to UV spectroscopy. Mater Sci Eng C 61: 56-62. http://dx.doi.org/10.1016/j.msec.2015.12.008.

Plasticized PVC is widely used to make medical devices such as tubing, perfusion bags and blood bags. By using confocal Raman microscopy on a PVC sheet plasticized with around 40% of di-(2-ethylhexyl)phthalate (DEHP), we propose a simple and sensitive approach to studying and understanding the diffusion of plasticizers from polymers into the surrounding media. Moreover, we sought to correlate our findings to standard measurements conducted by UV spectroscopy. This study showed differences in the concentration gradient observed due to the diffusion of the plasticizer inside a PVC sheet. We can thus follow the critical DEHP ratios that can impact the diffusion process. Water and ethanol were chosen as storage media: in ethanol, the lowest concentration of DEHP was observed at the surface resulting in the formation of a less plasticized layer near the interface; unlike ethanol, PVC sheets stored in water showed a greater concentration of DEHP on the film surface as an exudation of DEHP onto the surface.

hero.3479519

Alexandre, KB; Mufhandu, HT; London, GM; Chakauya, E; Khati, M. (2016). Progress and Perspectives on HIV-1 microbicide development [Review]. Virology 497: 69-80. http://dx.doi.org/10.1016/j.virol.2016.07.004.

The majority of HIV-1 infections occur via sexual intercourse. Women are the most affected by the epidemic, particularly in developing countries, due to their socio-economic dependence on men and the fact that they are often victims of gender based sexual violence. Despite significant efforts that resulted in the reduction of infection rates in some countries, there is still need for effective prevention methods against the virus. One of these methods for preventing sexual transmission in women is the use of microbicides. In this review we provide a summary of the progress made toward the discovery of affordable and effective HIV-1 microbicides and suggest future directions. We show that there is a wide range of compounds that have been proposed as potential microbicides. Although most of them have so far failed to show protection in humans, there are many promising ones currently in pre-clinical studies and in clinical trials.

hero.3469247

Al-Saleh, I; Elkhatib, R; Al-Rajoudi, T; Al-Qudaihi, G. (2017). Assessing the concentration of phthalate esters (PAEs) and bisphenol A (BPA) and the genotoxic potential of treated wastewater (final effluent) in Saudi Arabia. Sci Total Environ 578: 440-451. http://dx.doi.org/10.1016/j.scitotenv.2016.10.207.

Plasticizers such as phthalate esters (PAEs) and bisphenol A (BPA) are highly persistent organic pollutants that tend to bio-accumulate in humans through the soil-plant-animal food chain. Some studies have reported the potential carcinogenic and teratogenic effects in addition to their estrogenic activities. Water resources are scarce in Saudi Arabia, and several wastewater treatment plants (WTPs) have been constructed

for agricultural and industrial use. This study was designed to: (1) measure the concentrations of BPA and six PAEs, dimethyl phthalate (DMP), diethyl phthalate (DEP), dibutyl phthalate (DBP), butyl benzyl phthalate (BBP), bis (2-ethylhexyl) phthalate (DEHP) and dioctyl phthalate (DOP), in secondary- and tertiary-treated wastewater collected from five WTPs in three Saudi cities for four to five weeks and (2) test their potential genotoxicity. Three genotoxicological parameters were used: % tail DNA (%T), tail moment (TM) and percentage micronuclei (%MN). Both DBP and DEHP were detected in all treated wastewater samples. DMP, DEP, BBP, DOP, and BPA were found in 83.3, 84.2, 79, 73.7 and 97.4% of the samples, respectively. The levels of DMP (p<0.001), DOP (p<0.001) and BPA (p=0.001) were higher in tertiary- treated wastewater than secondary-treated wastewater, perhaps due to the influence of the molecular weight and polarity of the chemicals. Both weekly sampling frequency and WTP locations significantly affected the variability in our data. Treated wastewater from Wadi Al-Araj was able to induce DNA damage (%T and TM) in human lymphoblastoid TK6 cells that was statistically higher than wastewater from all other WTPs and in untreated TK6 cells (negative control). %MN in samples from both Wadi Al-Araj and Manfouah did not differ statistically but was significantly higher than in the untreated TK6 cells. This study also showed that the samples of tertiary-treated wastewater had a higher genotoxicological potential to induce DNA damage than the samples of secondary-treated wastewater. BPA and some PAEs in the treated wastewater might have the potential to induce genetic damage, despite their low levels. Genotoxicity, however, may also have been due to the presence of other contaminants. Our preliminary findings should be of concern to Saudi agriculture because long-term irrigation with treated wastewater could lead to the accumulation of PAEs and BPA in the soil and ultimately reach the human and animal food chain. WTPs need to remove pollutants more efficiently. Until then, a cautious use of treated wastewater for irrigation is recommended to avoid serious health impacts on local populations.

hero.3469351

Alves, A; Covaci, A; Voorspoels, S. (2016). Are nails a valuable non-invasive alternative for estimating human exposure to phthalate esters? Environ Res 151: 184-194. http://dx.doi.org/10.1016/j.envres.2016.07.023.

Most human biomonitoring studies conducted in the past year for assessing the human exposure to phthalate esters (PEs) employed measurements of PE metabolites in urine. Although urine is recognized as a valuable non-invasive matrix, it has also limitations regarding the short time window for exposure. Therefore, in this pilot feasibility study we aimed to assess the human exposure to seven PE metabolites (including mono(2-ethylhexyl) phthalate (MEHP), mono(2-ethyl-5-oxohexyl) phthalate (5-oxo-MEHP), mono(2-ethyl-5-hydroxyhexyl) phthalate (5-OH-MEHP), mono-n-butyl phthalate (MnBP), mono-isobutyl phthalate (MiBP), monoethyl phthalate (MEP) and mono-benzyl phthalate (MBzP)) using human nails. Paired nails and urine samples from the same individuals were used for comparison. Median levels of specific PE metabolites measured in nails and in spot urine of twenty Belgian individuals ranged from <LOQm to 146ng/g and from 0.2 to 6.7ng/mL (creatinine adjusted), respectively. The major PE metabolites found in nails were MEHP (average 146ng/g), sum (MnBP, MiBP) (average 212ng/g) and MEP (average 205ng/g). Significant correlations were achieved between different metabolites in nails and urine, i.e., MEHP levels in nails correlate well with sum (MnBP, MiBP) (r=0.73, p <0.01) and with MBzP (r=0.52, p <0.05) levels in urine. Moderate correlations were observed between 5-OH-MEHP and sum (MnBP, MiBP) (r=0.62, p <0.01) as well as with MEP (r=0.56, p <0.05) in both matrices. However, no significant correlation was observed for the same metabolite measured in both matrices. Based on participant questionnaires and after performing multivariate statistics, the relevant parameters of exposure positively associated with PE metabolites in nails were the use of hand care products, weight of the individuals and sport activity hours. Based on the detected levels and aforementioned predictors, nails seem a valuable non-invasive matrix for estimating human long-term exposure to DEP, DBnP and/or DIBP and DEHP.

hero.3469303

Alves, A; Koppen, G; Vanermen, G; Covaci, A; Voorspoels, S. (2016). Long-term exposure assessment to phthalates: How do nail analyses compare to commonly used measurements in urine. J Chromatogr B Analyt Technol Biomed Life Sci 1036-1037: 124-135. http://dx.doi.org/10.1016/j.jchromb.2016.09.039.

Phthalate esters (PEs) are easily metabolized and commonly excreted via urine within 24h, therefore their bioaccumulation potential is thought to be rather low. In the present study, we developed a sample preparation combined with a new microextraction method to measure seven PE metabolites in nails. The use

of whole nails did not result in significantly different levels compared to powdered nails, which makes the method very fast and user friendly. The method was validated using whole nails showing good accuracy, satisfactory precision and low limits of quantification (2-14ng/g). Although method development was the primary aim of the study, the method was also applied to real samples. PEs were measured in nails of 9 individuals collected at 2 distinct time points (15 days apart) and compared to levels in the respective urine samples (daily morning sample for 15 days). Additionally two volunteers have collected two more urine spots (afternoon and evening) per day. Major metabolites in nails were mono (ethyl hexyl) phthalate (MEHP), monoethyl phthalate (MEP) and sum of mono-n-butyl and mono-isobutyl phthalate (Σ(MnBP, MiBP)) while MEP and Σ(MnBP, MiBP) were the major ones identified in urine. In urine, first void morning urine reflected higher total excretion (sum of PEs of 7.0µg/g creatinine) for all individuals than the afternoon/evening voids. Participants also filled a questionnaire regarding their life-style. The use of hand care products and consumption of pre-packed food was associated with di-(2-ethylhexyl) phthalate (DEHP) oxidative metabolites, while the use of medical devices with butylbenzyl phthalate (BBzP) exposure. Although the metabolism (rate) and other factors that influence the transfer of the analytes from blood or other body compartments into nails needs further investigation, nails can be used to assess exposure to PEs. From our knowledge, urine reflects the excretion of PEs on 'daily basis' while nails show less fluctuation and more stable levels.

hero.3350194

Alves, A; Vanermen, G; Covaci, A; Voorspoels, S. (2016). Ultrasound assisted extraction combined with dispersive liquid-liquid microextraction (US-DLLME)-a fast new approach to measure phthalate metabolites in nails. Anal Bioanal Chem 408: 6169-6180. http://dx.doi.org/10.1007/s00216-016-9727-1.

A new, fast, and environmentally friendly method based on ultrasound assisted extraction combined with dispersive liquid-liquid microextraction (US-DLLME) was developed and optimized for assessing the levels of seven phthalate metabolites (including the mono(ethyl hexyl) phthalate (MEHP), mono(2-ethyl-5-hydroxyhexyl) phthalate (5-OH-MEHP), mono(2-ethyl-5-oxohexyl) phthalate (5-oxo-MEHP), mono-n-butyl phthalate (MnBP), mono-isobutyl phthalate (MiBP), monoethyl phthalate (MEP), and mono-benzyl phthalate (MBzP)) in human nails by UPLC-MS/MS. The optimization of the US-DLLME method was performed using a Taguchi combinatorial design (L9 array). Several parameters such as extraction solvent, solvent volume, extraction time, acid, acid concentration, and vortex time were studied. The optimal extraction conditions achieved were 180µL of trichloroethylene (extraction solvent), 2mL trifluoroacetic acid in methanol (2M), 2h extraction and 3min vortex time. The optimized method had a good precision (6-17%). The accuracy ranged from 79 to 108% and the limit of method quantification (LOQm) was below 14ng/g for all compounds. The developed US-DLLME method was applied to determine the target metabolites in 10 Belgian individuals. Levels of the analytes measured in nails ranged between <12 and 7982ng/g. The MEHP, MBP isomers, and MEP were the major metabolites and detected in every sample. Miniaturization (low volumes of organic solvents used), low costs, speed, and simplicity are the main advantages of this US-DLLME based method. Graphical Abstract Extraction and phase separation of the US-DLLME procedure.

hero.2816861

Aly, HAA; Hassan, MH; El-Beshbishy, HA; Alahdal, AM; Osman, AMM. (2015). Dibutyl phthalate induces oxidative stress and impairs spermatogenesis in adult rat. Toxicol Ind Health 32: 1467-1477. http://dx.doi.org/10.1177/0748233714566877.

Phthalates are abundantly produced plasticizers, and dibutyl phthalate (DBP) is the most widely used derivative in various consumer products and medical devices. This study was conducted to further explore the potential testicular toxicity of DBP in adult rats and to elucidate the underlying mechanisms. Adult male albino rats were treated orally with DBP at doses of 0, 200, 400, or 600 mg/kg/day for 15 consecutive days. Testicular weight, sperm count, and motility were significantly decreased. Treatment with DBP decreased serum follicle-stimulating hormone and testosterone levels and testicular lactate dehydrogenase activity. DBP treatment also decreased serum total antioxidant capacity and the activities of the testicular antioxidant enzymes, such as superoxide dismutase, catalase, and glutathione reductase. Further, DBP treatment provoked degeneration with absence of spermatogenesis and sperms and necrosis in some of seminiferous tubules. These results indicated that oxidative stress and subsequent decrease in testosterone secretion were the potential underlying mechanism of DBP-induced testicular toxicity.

hero.3479532

Amaral, S; S Tavares, R; Baptista, M; Sousa, MI; Silva, A; Escada-Rebelo, S; Paiva, CP; Ramalho-Santos, J. (2016). Mitochondrial Functionality and Chemical Compound Action on Sperm Function [Review]. Curr Med Chem 23: 3575-3606.

During the last decade, several studies have shown that mitochondrial parameters, such as integrity, respiratory activity, membrane potential and ROS production are intimately linked with sperm quality. Given the limitations of conventional semen analyses in terms of predicting male fertility, an increasing number of studies are focusing on the characterization of sperm mitochondria in order to more accurately assess sperm functionality. Moreover, mitochondria from several organs, such as the liver, have been described as a powerful screening tool for drug safety, being an easy in vitro model to assess the toxicity of distinct families of compounds. Given that mitochondrial functionality is intimately related to sperm homeostasis, it has become important to understand how compounds, ranging from dietary supplements, environmental pollutants, dependency-inducing drugs to pharmacological agents (such as erectile dysfunction-targeted drugs and male contraceptives) affect sperm mitochondrial function. In this review, we discuss studies describing the effects of various chemical agents on spermatozoa, with particular emphasis on mitochondrial function. From the extensive literature analyzed, we conclude that in some cases the role of sperm mitochondria as putative predictors of sperm functionality is very obvious, while in others further studies are needed to clarify this issue.

hero.3469306

Anand, K; Tiloke, C; Phulukdaree, A; Ranjan, B; Chuturgoon, A; Singh, S; Gengan, RM. (2016). Biosynthesis of palladium nanoparticles by using Moringa oleifera flower extract and their catalytic and biological properties. J Photochem Photobiol B, Biol 165: 87-95. http://dx.doi.org/10.1016/j.jphotobiol.2016.09.039.

The biosynthesis of nanostructured biopalladium nanoparticles (PdNPs) from an aqueous solution of crystalline palladium acetate is reported. For the synthesised PdNPs in solution, an agroforest biomass waste petal of Moringa oleifera derived bis-phthalate was used as natural reducing and biocapping agents. Continuous absorption in the UV region and subsequent brown colour change confirmed the formation of PdNPs. A strong surface plasmon peak for PdNPs occurred at 460nm. PdNPs were characterized by SEM with EDX, FTIR, TEM and DLS. The chemical composition of the aqueous extract was determined by GC-MS coupled with FTIR and (1)NMR. The catalytic degradation effect by PdNPs on industrial organic toxic effluents p-nitrophenol (PNP) and methylene blue dye was monitored by UV Spectroscopy. On the other hand PdNPs catalysed the base mediated suzuki coupling reaction for biphenyl synthesis, in water. Moreover, PdNPs were found to be reusable catalysts. Toxicity studies of PdNPs showed that the death of brine shrimp to be <50%. Therefore, PdNPs displayed potential for further anticancer studies via tumour cell lines. The in vitro cytotoxicity evaluation of the extract capped nanoparticles was carried out using human lung carcinoma cells (A549) and peripheral lymphocytes normal cells by MTT cell viability assay. Also, PdNPs showed antibacterial activity against Enterococcus faecalis among the different tested strains, including Bacillus cereus, Staphylococcus aureus, Esherichia coli and Candida albicans, Candida utilis.

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Araki, A; Mitsui, T; Goudarzi, H; Nakajima, T; Miyashita, C; Itoh, S; Sasaki, S; Cho, K; Moriya, K; Shinohara, N; Nonomura, K; Kishi, R. (2016). Prenatal di(2-ethylhexyl) phthalate exposure and disruption of adrenal androgens and glucocorticoids levels in cord blood: The Hokkaido Study. Sci Total Environ. http://dx.doi.org/10.1016/j.scitotenv.2016.12.124.

Di(2-ethylhexyl) phthalate (DEHP) is known for its endocrine disrupting properties. We previously demonstrated that prenatal DEHP exposure is associated with decreased progesterone levels and testosterone/estradiol ratio in the cord blood. However, evidence of the effects of prenatal DEHP exposure on adrenal androgen and glucocorticoids in infants is scarce. Thus, the objectives of this study were to investigate the association between prenatal DEHP exposure and adrenal androgen and glucocorticoids, and to discuss its effects on steroid hormone profiles in infants. This is part of a birth cohort study: The Hokkaido Study on Environment and Children's Health, Sapporo Cohort. Among the 514 participants, 202 mother-infant pairs with available data on maternal mono(2-ethylhexyl) phthalate (MEHP), adrenal androgen (dehydroepiandrostenedione [DHEA] and androstenedione) and glucocorticoid (cortisol and cortisone) cord

blood levels were included in this study. After adjusting for potential confounders, a linear regression analysis showed that maternal MEHP levels were associated with reduced cortisol and cortisone levels and glucocorticoid/adrenal androgen ratio, whereas increased DHEA levels and DHEA/androstenedione ratio. In a quartile model, when comparing the adjusted least square means in the 4th quartile of MEHP with those in the 1st quartile, cortisol and cortisone levels and glucocorticoid/adrenal androgen ratio decreased, whereas DHEA/androstenedione and cortisol/cortisone ratios increased. Significant p-value trends for cortisol and cortisone levels, cortisol/cortisone ratio, and glucocorticoid/adrenal androgen ratio were observed. In combination with the previous results of reduced progesterone levels and testosterone/estradiol ratio, prenatal exposure to DEHP altered the steroid hormone profiles of infants. Further studies investigating the long-term effects of DEHP exposure on growth, neurodevelopment, and gonad and reproductive function are required.

hero.3469485

Arbuckle, TE; Davis, K; Boylan, K; Fisher, M; Fu, J. (2016). Processed data for CHMS 2007-2009: Bisphenol A, phthalates and lead and learning and behavioral problems in Canadian children 6-19 years of age. 8: 784-802. http://dx.doi.org/10.1016/j.dib.2016.06.017.

This article presents processed data from an analysis of cross-sectional data from Cycle 1 of the Canadian Health Measures Survey (CHMS) to examine the potential association between urinary concentrations of BPA and phthalate metabolites and child learning and behavioral problems, considering important covariates such as gender, blood lead and environmental tobacco smoke (ETS). These processed data are related to the research on a subset of the children (Arbuckle et al., 2016) [1]. The Strengths and Difficulties Questionnaire (SDQ) outcomes of interest were emotional symptoms, hyperactivity/inattention, and a total difficulties SDQ score, with borderline and abnormal scores grouped together and compared with children with normal scores. Other outcomes studied included reported learning disability, ADD/ADHD (attention deficit disorder/attention deficit hyperactivity disorder) and use of psychotropic medications to treat behavioral disorders in the past month. Data are presented for all children 6-19 years of age combined. Weighted simple logistic regression estimates for important covariates of each of the outcomes from CHMS Cycle 1 children are reported. Odds ratios based on weighted multiple logistic regression estimates for urinary BPA and phthalate metabolites (including specific gravity as a covariate) and blood lead are presented for the reported outcomes ADD/ADHD, learning disability and psychotropic medications, as well as the SDQ outcomes emotional symptoms, hyperactivity/inattention and total difficulties.

hero.3479512

Arfi, A; Cohen, J; Canlorbe, G; Bendifallah, S; Thomassin-Naggara, I; Darai, E; Benachi, A; Arfi, JS. (2016). First-trimester determination of fetal gender by ultrasound: measurement of the ano-genital distance. Eur J Obstet Gynecol Reprod Biol 203: 177-181. http://dx.doi.org/10.1016/j.ejogrb.2016.06.001.

INTRODUCTION: Early ultrasound fetal sex determination is of obvious interest, particularly in the context of X-linked diseases. In the human, the anogenital distance, i.e., the distance between the caudal end and the base of the genital tubercule is sexually dimorphic. This difference is apparent from 11 weeks of gestation. The aim of this prospective study was to evaluate the accuracy of anogenital distance measurement during the first trimester ultrasound in the early determination of fetal gender.

MATERIALS AND METHODS: Fetal gender was assessed by ultrasound in 310 singleton pregnancies at 11-14 weeks of gestation. The optimal cut-off was determined by the minimal p-value technic and validated using bootstrap simulation.

RESULTS: 310 women were included. A cut-off of 4.8mm was determined to predict male (4.8mm) or female (<4.8mm) fetuses. Sex was correctly determined for 87% of the males and 89% of the females. The inter-observer variability was excellent.

CONCLUSION: This study presents a new sonographic sign for early fetal sex determination that has not been previously explored. It appears to be an accurate tool but it requires further validation in larger series.

hero.3469372

Aylward, LL; Hays, SM; Zidek, A. (2016). Variation in urinary spot sample, 24 h samples, and longer-term average urinary concentrations of short-lived environmental chemicals: implications for exposure assessment and reverse dosimetry. J Expo Sci Environ Epidemiol. http://dx.doi.org/10.1038/jes.2016.54.

Population biomonitoring data sets such as the Canadian Health Measures Survey (CHMS) and the United States National Health and Nutrition Examination Survey (NHANES) collect and analyze spot urine samples for analysis for biomarkers of exposure to non-persistent chemicals. Estimation of population intakes using such data sets in a risk-assessment context requires consideration of intra- and inter-individual variability to understand the relationship between variation in the biomarker concentrations and variation in the underlying daily and longer-term intakes. Two intensive data sets with a total of 16 individuals with collection and measurement of serial urine voids over multiple days were used to examine these relationships using methyl paraben, triclosan, bisphenol A (BPA), monoethyl phthalate (MEP), and mono-2-ethylhexyl hydroxyl phthalate (MEHHP) as example compounds. Composited 24 h voids were constructed mathematically from the individual collected voids, and concentrations for each 24 h period and average multiday concentrations were calculated for each individual in the data sets. Geometric mean and 95th percentiles were compared to assess the relationship between distributions in spot sample concentrations and the 24 h and multiday collection averages. In these data sets, spot sample concentrations at the 95th percentile were similar to or slightly higher than the 95th percentile of the distribution of all 24 h composite void concentrations, but tended to overestimate the maximum of the multiday concentration averages for most analytes (usually by less than a factor of 2). These observations can assist in the interpretation of population distributions of spot samples for frequently detected analytes with relatively short elimination half-lives.Journal of Exposure Science and Environmental Epidemiology advance online publication, 5 October 2016; doi:10.1038/jes.2016.54.

hero.3469431

Balachandar, S; Sethuram, M; Muthuraja, P; Shanmugavadivu, T; Dhandapani, M. (2016). Ligand based pharmacophoric modelling and docking of bioactive pyrazolium 3-nitrophthalate (P3NP) on Bacillus subtilis, Aspergillus fumigatus and Aspergillus niger - Computational and Hirshfeld surface analysis. J Photochem Photobiol B, Biol 163: 352-365. http://dx.doi.org/10.1016/j.jphotobiol.2016.08.045.
Biologically active Lewis acid-base compound, pyrazolium 3-nitro phthalate (P3NP) has been synthesized and crystallized by slow evaporation - solution method at 30C. Spectral and single crystal X-Ray diffraction (XRD) were used to characterize the compound. The stability of the P3NP was confirmed by UV-Visible spectral analysis. P3NP crystallizes in monoclinic P21/C space group with cell parameters, a=13.009 (3) Å, b=12.584 (3) Å, c=7.529 (18) Å and β=93.052 (4)(o) with Z=4. Crystal packing was stabilized by N(+)HO(-), OHO and CHO intermolecular hydrogen bonds. The nature of anion - cation interactions and crystal packing from various types of intermolecular contacts and their importance were explored using the Hirshfeld surface analysis. The structure was optimized by Density Functional Theory at B3LYP level with 6-311++G(d,p) basis set and the vibrational frequencies were theoretically calculated. Band gap between Highest Occupied Molecular Orbital (HOMO) and Lowest Unoccupied Molecular Orbital (LUMO) and Electrostatic potential (ESP) were calculated. Antimicrobial activities of P3NP with targets were clinically tested and were found to exhibit antibacterial activity against gram positive and antifungal activity against pathogens with Minimum Inhibitory Concentration (MIC). Ligand based pharmacophore modelling was used to understand the potential of P3NP ligand to bind with selected target proteins. iGEM Dock was used to predict the modes of interactions of the ligand with target proteins of the microbes predicted from pharmacophore. PreADMET predicts no absorption of ligand in Human Intestinal Absorption (HIA).

hero.3479545

Bardak, F; Karaca, C; Bilgili, S; Atac, A; Mavis, T; Asiri, AM; Karabacak, M; Kose, E. (2016). Conformational, electronic, and spectroscopic characterization of isophthalic acid (monomer and dimer structures) experimentally and by DFT. Spectrochim Acta A Mol Biomol Spectrosc 165: 33-46. http://dx.doi.org/10.1016/j.saa.2016.03.050.
Isophthalic acid (C6H4(CO2H)2) is a noteworthy organic compound widely used in coating and synthesis of resins and the production of commercially important polymers such as drink plastic bottles. The effects of isophthalic acid (IPA) on human health, toxicology, and biodegradability are the main focus of many researchers. Because structural and spectroscopic investigation of molecules provides a deep understanding of interactional behaviors of compounds, this study stands for exploring those features. Therefore, the spectroscopic, structural, electronic, and thermodynamical properties of IPA were thoroughly studied in this work experimentally using UV-Vis, (1)H and (13)C NMR, FT-IR, FT-Raman and theoretically via DFT and TD-DFT calculations. The UV-Vis absorption spectrum in water was taken in the region 200-400nm. The NMR

chemical shifts ((1)H and (13)C) were recorded in DMSO solution. The infrared and Raman spectra of the solid IPA were recorded in the range of 4000-400cm(-1) and 3500-50cm(-1), respectively. DFT and TD-DFT calculations were performed at the level of B3LYP/6-311++G(d,p) in determination of geometrical structure, electronic structure analysis and normal mode. The (13)C and (1)H nuclear magnetic resonance (NMR) spectra were estimated by using the gauge-invariant atomic orbital (GIAO) method. The scaled quantum mechanics (SQM) method was used to determine the total energy distribution (TED) to assign the vibrational modes accurately. Weak interactions such as hydrogen bonding and Van der Walls were analyzed via reduced density gradient (RDG) analysis in monomeric and dimeric forms. Furthermore, the excitation energies, density of state (DOS) diagram, thermodynamical properties, molecular electro-static potential (MEP), and nonlinear optical (NLO) properties were obtained.

hero.3479524

Benjamin, S; Kamimura, N; Takahashi, K; Masai, E. (2016). Achromobacter denitrificans SP1 efficiently utilizes 16 phthalate diesters and their downstream products through protocatechuate 3,4-cleavage pathway. Ecotoxicol Environ Saf 134P1: 172-178. http://dx.doi.org/10.1016/j.ecoenv.2016.08.028.

This study provides physical and analytical evidences for the efficient utilization of most of the commercially available phthalate diesters by Achromobacter denitrificans SP1, coupled with the demonstration of a plausible degradation pathway. We tested 17 phthalate diesters [viz., ditridecyl phthalate, diisodecyl phthalate (DIDP), di(2-ethylhexyl)phthalate (DEHP), di-n-octyl phthalate (DOP), bis(2-ethylhexyl)isophthalate (BEIP), dihexyl phthalate (DHP), dibutyl phthalate (DBP), dicyclohexyl phthalate (DCHP), diphenyl phthalate (DPP), benzyl butyl phthalate (BBP), diamyl phthalate (DAmP), diisobutyl phthalate, dipropyl phthalate, dially phthalate (DAlP), diethyl phthalate, diethyl terephthalate and dimethyl phthalate (DMP)], and their major degradation products for the degradation efficiency of A. denitrificans SP1 in Wx medium. It efficiently utilized 16 phthalate diesters (except DAlP), and showed general preference toward phthalate diesters with longer side chains (utilized ~10mM in 48h) than those with shorter side chains and with cyclic structures (utilized ~5mM in 48h) accompanied by a sharp decline of pH to ~5 from initial 7. In a detailed study, about 37mM (~15g/L) DEHP was utilized in 48h. Moreover, A. denitrificans SP1 produced reddish-pink pigment when DIDP, DEHP, DOP, DHP, DBP, DIBP, BBP, DAmP, DCHP, DPP or DMP was supplied in the medium. From the available evidences, it seems that its putative phthalate diester degradation pathway contains the following check points: phthalate diesters, phthalate monoesters, phthalate (4,5-dioxygenase), protocatechuate (3,4-dioxygenase), and TCA cycle. Nonspecificity toward utilization of phthalate diesters, especially with greater specificity to phthalate diesters having longer side chain, and the characteristic sticky reddish-pink (or colorless) cell clump formation in the presence of phthalate diesters makes A. denitrificans SP1 a very attractive candidate to be employed as an efficient biofactory in waste water treatment processes.

hero.3469382

Berman, T; Goldsmith, R; Levine, H; Grotto, I. (2016). Human biomonitoring in Israel: Recent results and lessons learned [Review]. Int J Hyg Environ Health. http://dx.doi.org/10.1016/j.ijheh.2016.09.008.

The use of human biomonitoring (HBM) as a tool for environmental health policy and research is developing rapidly in Israel. Despite challenges in securing political and financial support for HBM, the Ministry of Health has initiated national HBM studies and has utilized HBM data in environmental health policy decision making. Currently, the Ministry of Health is collecting urine samples from children and adults in the framework of the National Health and Nutrition Study (MABAT), with the goal of ongoing surveillance of population exposure to pesticides and environmental tobacco smoke, and of combining HBM data with data on diet and health behavior. In academic research studies in Israel, biomarkers are used increasingly in environmental epidemiology, including in three active birth cohort studies on adverse health effects of phthalates, brominated flame retardants, and organophosphate pesticides. Future Ministry of Health goals include establishing HBM analytical capabilities, developing a long term national HBM plan for Israel and participating in the proposed HBM4EU project in order to improve data harmonization. One of the lessons learned in Israel is that even in the absence of a formal HBM program, it is possible to collect meaningful HBM data and use it in an ad hoc fashion to support environmental health policy.

hero.3469605

Bernard, L; Cueff, R; Chagnon, M; Abdoulouhab, F; Décaudin, B; Breysse, C; Kauffmann, S; Cosserant, B; Souweine, B;

Sautou, V; group, As. (2015). Migration of plasticizers from PVC medical devices: Development of an infusion model. Int J Pharm 494: 136-145. http://dx.doi.org/10.1016/j.ijpharm.2015.08.033.

Alternatives to DEHP plasticizers are used in various PVC medical devices (MD) for infusion. As they are able to migrate from these MDs into infused solutions, they may come into contact with patient. Different and specific clinical parameters influence their migration in at-risk situations such as infusion. In contrast to the regulations for Food Contact Materials (MCDA), there is currently no acceptable migration limits for the use of these plasticizers in clinical situations. In order to assess their migration, and thus control the risks linked to these MDs, we developed a migration model for the plasticizers in MDs. To this end, we applied a cross-disciplinary methodological process similar to that used in the food-processing industry, taking into account the MDs' conditions of use in clinical practice. The simulation model is simple and includes the following conditions: MD should be tested with a dynamic method that respects our established clinical assumption (2 L of infused solutions via 13 dm(2) of plasticized PVC), at a temperature of 25 C and during 24 h of contact, using a 50/50 (v/v) ethanol/water simulant. This model could be proposed as a tool for the safety evaluation of the patients' exposure risk to plasticizers from PVC medical devices for infusions.

hero.3469540

Boisvert, A; Jones, S; Issop, L; Erythropel, HC; Papadopoulos, V; Culty, M. (2016). In vitro functional screening as a means to identify new plasticizers devoid of reproductive toxicity. Environ Res 150: 496-512. http://dx.doi.org/10.1016/j.envres.2016.06.033.

Plasticizers are indispensable additives providing flexibility and malleability to plastics. Among them, several phthalates, including di (2-ethylhexyl) phthalate (DEHP), have emerged as endocrine disruptors, leading to their restriction in consumer products and creating a need for new, safer plasticizers. The goal of this project was to use in vitro functional screening tools to select novel non-toxic plasticizers suitable for further in vivo evaluation. A panel of novel compounds with satisfactory plasticizer properties and biodegradability were tested, along with several commercial plasticizers, such as diisononyl-cyclohexane-1,2-dicarboxylate (DINCH). MEHP, the monoester metabolite of DEHP was also included as reference compound. Because phthalates target mainly testicular function, including androgen production and spermatogenesis, we used the mouse MA-10 Leydig and C18-4 spermatogonial cell lines as surrogates to examine cell survival, proliferation, steroidogenesis and mitochondrial integrity. The most promising compounds were further assessed on organ cultures of rat fetal and neonatal testes, corresponding to sensitive developmental windows. Dose-response studies revealed the toxicity of most maleates and fumarates, while identifying several dibenzoate and succinate plasticizers as innocuous on Leydig and germ cells. Interestingly, DINCH, a plasticizer marketed as a safe alternative to phthalates, exerted a biphasic effect on steroid production in MA-10 and fetal Leydig cells. MEHP was the only plasticizer inducing the formation of multinucleated germ cells (MNG) in organ culture. Overall, organ cultures corroborated the cell line data, identifying one dibenzoate and one succinate as the most promising candidates. The adoption of such collaborative approaches for developing new chemicals should help prevent the development of compounds potentially harmful to human health.

hero.3449692

Bornman, MS; Chevrier, J; Rauch, S; Crause, M; Obida, M; Sathyanarayana, S; Barr, DB; Eskenazi, B. (2016). Dichlorodiphenyltrichloroethane exposure and anogenital distance in the Venda Health Examination of Mothers, Babies and their Environment (VHEMBE) birth cohort study, South Africa. Andrology 4: 608-615. http://dx.doi.org/10.1111/andr.12235.

Dichlorodiphenyltrichloroethane (DDT) is used for malaria control by 10 countries, nine of which are in Africa. Technical DDT contains various isomers with 65-80% insecticidal p,p'-DDT and 15-21% o,p'-DDT, an estrogenic chemical, while the persistent metabolite of p,p'-DDT, dichlorodiphenyldichloroethylene (p,p'-DDE), is an antiandrogen. In utero antiandrogenic exposure reduces anogenital distance in animal models and the anal position index in a single study. This study examined the associations between mother's serum DDT and DDE levels at delivery and anogenital distance in their children at birth and age 1year. Data were collected as part of the Venda Health Examination of Mothers, Babies and their Environment (VHEMBE), a birth cohort study located in rural South Africa. DDT and DDE concentrations were measured in blood samples collected from 752 mothers at delivery. Anogenital distance measurements, taken at birth (n=671) and age 1year (n=674), included anofourchette and anoclitoral distances in girls, and anoscrotal and

anopenile lengths in boys. We also measured anococcygeal and coccyx-fourchette distances in girls, while in boys, we measured anococcygeal and coccyx-scrotal distances as well as penile length and penile width. The anal position index is calculated for both sexes as anoscrotal/coccyx-scrotal in boys and anofourchette/coccyx-fourchette in girls. We found no associations between p,p'-DDT/-DDE or o,p'-DDT and anogenital distance measurements at birth in either boys or girls. At 1year, o,p'-DDE was negatively associated with anofourchette in girls (β=-1.32mm, 95% confidence interval (CI)=-2.27, -0.38) and positively associated with penile width in boys (β=0.30mm, 95% CI=0.00, 0.60). The results do not suggest an overt antiandrogenic or estrogenic effect on anogenital distance after long-term DDT exposure. These weak associations may be due to chance.

hero.3444888

Botton, J; Philippat, C; Calafat, AM; Carles, S; Charles, MA; Slama, R. (2016). Phthalate pregnancy exposure and male offspring growth from the intra-uterine period to five years of age. Environ Res 151: 601-609. http://dx.doi.org/10.1016/j.envres.2016.08.033.

OBJECTIVE: To study associations between prenatal exposure to phthalates and fetal and postnatal growth up to age 5 years in male offspring.

METHODS: Eleven phthalate metabolites were quantified in spot maternal urine samples collected during gestation among 520 women of the EDEN mother-child cohort who gave birth to a boy. Fetal growth was assessed from repeated ultrasound measurements and measurements at birth. We used repeated measures of weight and height in the first 5 years of life to model individual postnatal growth trajectories. We estimated adjusted variations in pre and postnatal growth parameters associated with an interquartile range increase in ln-transformed phthalate metabolite concentrations.

RESULTS: Monocarboxyisononyl phthalate (MCNP) was positively associated with femoral length during gestation and length at birth. High molecular weight phthalate metabolites were negatively associated with estimated fetal weight throughout pregnancy. Monoethyl phthalate (MEP) showed positive association with weight growth velocity from two to five years and with body mass index at five years (β=0.17kg/m(2), 95% confidence interval, 0.04, 0.30).

CONCLUSIONS: We highlighted associations between gestational exposure to some phthalates and growth in boys. The positive association between MEP and postnatal growth in boys was also reported in several previous human studies.

hero.3350193 REVIEW

Bowman, JD; Choudhury, M. (2016). Phthalates in neonatal health: friend or foe? J Dev Orig Health Dis 7: 1-13. http://dx.doi.org/10.1017/S2040174416000349.

Exposure to environmental chemicals has adverse effects on the health and survival of humans. Emerging evidence supports the idea that exposure to endocrine-disrupting compounds (EDCs) can perturb an individual's physiological set point and as a result increase his/her propensity toward several diseases. The purpose of this review is to provide an update on di-(2-ethylhexyl) phthalate, the primary plasticizer found in plastic medical devices used in neonatal intensive care units, its effects on the fetus and newborn, epidemiological studies, pharmacokinetics, toxicity and epigenetic implications. We searched the PubMed databases to identify relevant studies. Phthalates are known EDCs that primarily are used to improve the flexibility of polyvinyl chloride plastic products and are called plasticizers in lay terms. Neonates and infants are particularly vulnerable to the effects of phthalates, beginning with maternal exposure and placental transfer during gestation and during infancy following birth. In line with the developmental origins of adult disease, a focus on the effects of environmental chemicals in utero or early childhood on the genesis of adult diseases through epigenome modulation is timely and important. The epigenetic effects of phthalates have not been fully elucidated, but accumulating evidence suggests that they may be associated with adverse health effects, some of which may be heritable. Phthalate exposure during pregnancy and the perinatal period is particularly worrisome in health-care settings. Although the clinical significance of phthalate exposure has been difficult to assess with epidemiologic studies, the evidence that physiological changes occur due to exposure to phthalates is growing and points toward the need for more investigation at a molecular, specifically epigenetic level.

hero.3469233 REVIEW

Braun, JM. (2016). Early-life exposure to EDCs: role in childhood obesity and neurodevelopment [Review]. Nat Rev

Endocrinol. http://dx.doi.org/10.1038/nrendo.2016.186.
Endocrine-disrupting chemicals (EDCs) might increase the risk of childhood diseases by disrupting hormone-mediated processes that are critical for growth and development during gestation, infancy and childhood. The fetus, infant and child might have enhanced sensitivity to environmental stressors such as EDCs due to their rapid development and increased exposure to some EDCs as a consequence of development-specific behaviour, anatomy and physiology. In this Review, I discuss epidemiological studies examining the relationship between early-life exposure to bisphenol A (BPA), phthalates, triclosan and perfluoroalkyl substances (PFAS) with childhood neurobehavioural disorders and obesity. The available epidemiological evidence suggest that prenatal exposure to several of these ubiquitous EDCs is associated with adverse neurobehaviour (BPA and phthalates) and excess adiposity or increased risk of obesity and/or overweight (PFAS). Quantifying the effects of EDC mixtures, improving EDC exposure assessment, reducing bias from confounding, identifying periods of heightened vulnerability and elucidating the presence and nature of sexually dimorphic EDC effects would enable stronger inferences to be made from epidemiological studies than currently possible. Ultimately, improved estimates of the causal effects of EDC exposures on child health could help identify susceptible subpopulations and lead to public health interventions to reduce these exposures.

hero.3466599

Braun, JM; Bellinger, DC; Hauser, R; Wright, RO; Chen, A; Calafat, AM; Yolton, K; Lanphear, BP. (2016). Prenatal phthalate, triclosan, and bisphenol A exposures and child visual-spatial abilities. Neurotoxicology 58: 75-83. http://dx.doi.org/10.1016/j.neuro.2016.11.009.
INTRODUCTION: During fetal development, sex steroids influence sexually dimorphic behaviors, such as visual-spatial abilities. Thus, endocrine disrupting chemicals that impact sex steroids during gestation may affect these behaviors.

OBJECTIVE: We investigated the relationship between prenatal urinary phthalate metabolite, triclosan, and BPA concentrations and visual-spatial abilities in a prospective cohort of 198 mother-child dyads.

METHODS: Data are from a prospective cohort in Cincinnati, OH (HOME Study). We measured nine phthalate metabolites, triclosan, and BPA in maternal urine samples collected at 16 and 26 weeks of gestation. We assessed children's visual-spatial abilities at 8 years of age using the Virtual Morris Water Maze (VMWM), a computerized version of the rodent Morris Water Maze. We quantified the covariate-adjusted change in the time or distance to complete the VMWM and time spent in the correct quadrant during a probe trial with an interquartile range increase in chemical concentrations using linear mixed models and linear regression, respectively.

RESULTS: Boys completed the VMWM faster (4.1s; 95% CI:-7.1, -1.2) and in less distance (1.4 units; 95% CI:-2.8, 0) than girls. Overall, children with higher mono-n-butyl (MnBP), mono-benzyl (MBzP), and mono-carboxypropyl phthalate concentrations completed the VMWM in less time and distance than children with lower concentrations. For example, children with higher MnBP concentrations completed the VMWM in 0.9 less distance units (95% CI:-1.8, -0.0). Child sex modified the association between MnBP and VMWM performance. In girls, higher MnBP concentrations were associated with longer time (1.7s; 95% CI: -0.7, 4.1) and shorter distance (-1.7 units; 95% CI: -2.8, -0.5), whereas in boys, it was associated with shorter time (-3.0s; 95% CI:-5.6, -0.4), but not distance (-0.1 units; 95% CI:1.4, 1.0). Other phthalate metabolites, triclosan, and BPA were not associated with VMWM performance, and sex did not consistently modify these associations.

CONCLUSIONS: In this cohort, greater prenatal urinary concentrations of some phthalate metabolites were associated with improved VMWM performance, particularly among boys. Future studies should confirm these findings and determine if phthalates affect other hormonally sensitive aspects of child neurobehavior.

hero.3469268

Buluş, AD; Aşci, A; Erkekoglu, P; Balci, A; Andiran, N; Koçer-Gümüşel, B. (2016). The evaluation of possible role of endocrine disruptors in central and peripheral precocious puberty. Toxicol Mech Meth 26: 493-500. http://dx.doi.org/10.3109/15376516.2016.1158894.
Exposure to environmental chemicals can affect genetic and epigenetic molecular pathways and may cause altered growth and development. Among those exposures, endocrine-disrupting chemicals (EDCs) are of particular concern as humans are abundantly exposed to these chemicals by various means in every period of life. Several well-known environmental chemicals, including phthalates and bisphenol A (BPA), are

classified as EDCs. These EDCs are suggested to play roles in early onset of puberty in girls. The aim of this study is to determine plasma phthalate (di(2-ethylhexyl)phthalate [DEHP] and its main metabolite mono(2-ethylhexyl)phthalate [MEHP]) and urinary BPA levels in girls with idiopathic central precocious puberty (CPP) and peripheral precocious puberty (PPP). This study was performed on newly diagnosed idiopathic central precocious puberty (CPP) patients (n = 42) and peripheral precocious puberty (PPP) (n = 42) patients, who were admitted to Keçiören Training and Research Hospital, Clinic of Pediatric Endocrinology between August 2012 and -July 2013. Nonobese healthy girls (n = 50) were used as the control group. Urinary BPA levels were not statistically different in control, PPP and CPP groups (medians 10.91, 10.63 and 10.15 µg/g creatinine, respectively; p > 0.05). Plasma DEHP levels were significantly higher in PPP group when compared to control. Plasma MEHP levels were not significantly different in control and PPP groups (p > 0.05). However, in CPP group, both plasma DEHP and MEHP levels were significantly higher than control and PPP groups. This study showed that phthalates might play a role in the occurence of CPP in girls.

hero.3479500

Calafat, AM; Baker, SE; Wong, LY; Bishop, AM; Morales-A, P; Valentin-Blasini, L. (2016). Novel exposure biomarkers of N,N-diethyl-m-toluamide (DEET): Data from the 2007-2010 National Health and Nutrition Examination Survey. Environ Int 92-93: 398-404. http://dx.doi.org/10.1016/j.envint.2016.04.021.
BACKGROUND: N,N-diethyl-m-toluamide (DEET) is a widely used insect repellent in the United States.

OBJECTIVES: To assess exposure to DEET in a representative sample of persons 6years and older in the U.S. general population from the 2007-2010 National Health and Nutrition Examination Survey.

METHODS: We analyzed 5348 urine samples by using online solid-phase extraction coupled to isotope dilution-high-performance liquid chromatography-tandem mass spectrometry. We used regression models to examine associations of various demographic parameters with urinary concentrations of DEET biomarkers.

RESULTS: We detected DEET in ~3% of samples and at concentration ranges (>0.08µg/L-45.1µg/L) much lower than those of 3-(diethylcarbamoyl)benzoic acid (DCBA) (>0.48µg/L-30,400µg/L) and N,N-diethyl-3-hydroxymethylbenzamide (DHMB) (>0.09µg/L-332µg/L). DCBA was the most frequently detected metabolite (~84%). Regardless of survey cycle and the person's race/ethnicity or income, adjusted geometric mean concentrations of DCBA were higher in May-Sep than in Oct-Apr. Furthermore, non-Hispanic whites in the warm season were more likely than in the colder months [adjusted odds ratio (OR)=10.83; 95% confidence interval (CI), 3.28-35.79] and more likely than non-Hispanic blacks (OR=3.45; 95% CI, 1.51-7.87) to have DCBA concentrations above the 95th percentile.

CONCLUSIONS: The general U.S. population, including school-age children, is exposed to DEET. However, reliance on DEET as the sole urinary biomarker would likely underestimate the prevalence of exposure. Instead, oxidative metabolites of DEET are the most adequate exposure biomarkers. Differences by season of the year based on demographic variables including race/ethnicity likely reflect different lifestyle uses of DEET-containing products.

hero.3469291

Calafat, AM; Ye, X; Valentin-Blasini, L; Li, Z; Mortensen, ME; Wong, LY. (2016). Co-exposure to non-persistent organic chemicals among American pre-school aged children: A pilot study. Int J Hyg Environ Health. http://dx.doi.org/10.1016/j.ijheh.2016.10.008.
BACKGROUND: General population human biomonitoring programs such as the National Health and Nutrition Examination Survey (NHANES) in the United States suggest that chemical exposures are common. Exposures during childhood may affect health later in life, but biomonitoring data in NHANES among pre-school aged children are limited.

METHODS: A convenience group of 122 3-5year old American boys and girls were recruited in 2013 for a pilot study to assess the feasibility of collecting urine from young children and analyzing it for select chemical exposure biomarkers for future NHANES. Children were primarily Hispanic (64.8%); the remainder was divided between non-Hispanic black, and non-Hispanic white and "other." We measured 52 urinary biomarkers: 13 phthalates and one non-phthalate plasticizer, five phenols and four parabens, 10 polycyclic aromatic hydrocarbons (PAHs), and 19 pesticides. For each biomarker, we calculated descriptive statistics. We also calculated the number of biomarkers detected within each child, and performed principal components analysis (PCA).

RESULTS: NHANES staff obtained permission to

attempt collection of 60mL urine from 3 to 5year olds who participated in the 2013 NHANES health examination; 83% of children successfully provided the target volume. We detected 24 individual biomarkers of pesticides, phenols and parabens, phthalates/non-phthalate plasticizers, and PAHs in 95-100% of children. The median number of biomarkers detected was 37: nine pesticides, five phenols and parabens, 13 phthalates and non-phthalate plasticizers, and 10 PAHs. Biomarkers concentrations appear to be similar to national estimates among 6-11year old children from previous NHANES. PCA suggested high within-class correlations among biomarkers.

CONCLUSIONS: These young children successfully adhered to the collection protocol and produced enough urine for the quantification of environmental biomarkers currently being measured in NHANES participants 6 years of age and older. Using the same analytical methods employed for the analysis of samples collected from older NHANES participants, in this sample of pre-school aged children we detected multiple chemicals including plasticizers, combustion products, personal-care product chemicals, and pesticides. Starting with NHANES 2015-2016, the NHANES biomonitoring program will include urinary biomarkers for 3-5year old children to provide exposure data to select chemicals at the national level among this age group.

hero.3052882

Cao, XL; Zhao, W; Dabeka, R. (2015). Di-(2-ethylhexyl) adipate and 20 phthalates in composite food samples from the 2013 Canadian Total Diet Study. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 32: 1893-1901. http://dx.doi.org/10.1080/19440049.2015.1079742.

A sensitive and selective GC-MS method was developed and used for simultaneous analysis of di-(2-ethylhexyl) adipate (DEHA) and 20 selected phthalates in the food samples from the 2013 Canadian Total Diet Study. At least one of the 21 target chemicals was detected in 141 of the 159 different food composite samples analysed. However, only seven of the 21 target chemicals were detected, with di-(2-ethylhexyl) phthalate (DEHP) and DEHA being detected most frequently, in 111 and 91 different food composite samples, respectively, followed by di-n-butyl phthalate (DBP) (n = 44), n-butyl benzyl phthalate (BBzP) (32), di-iso-butyl phthalate (DiBP) (27), di-ethyl phthalate (DEP) (3), and di-cyclohexyl phthalate (DCHP) (1). Levels of DEP (di-ethyl phthalate), DiBP, DBP, BBzP and DCHP were low, in general, with average concentrations of 9.63, 8.26, 23.2, 12.4 and 64.9ngg(-1), respectively. Levels of DEHA and DEHP varied widely, ranging from 1.4 to 6010ngg(-1) and from 14.4 to 714ngg(-1), respectively. High levels of DEHA were found mainly in the composite samples where the individual food items used to prepare the composite were likely packaged in polyvinyl chloride (PVC) wrapping film, while the highest DEHP levels were found in the vegetable and fruit samples.

hero.3454978

Carter, CJ; Blizard, RA. (2016). Autism genes are selectively targeted by environmental pollutants including pesticides, heavy metals, bisphenol A, phthalates and many others in food, cosmetics or household products [Review]. Neurochem Int. http://dx.doi.org/10.1016/j.neuint.2016.10.011.

The increasing incidence of autism suggests a major environmental influence. Epidemiology has implicated many candidates and genetics many susceptibility genes. Gene/environment interactions in autism were analysed using 206 autism susceptibility genes (ASG's) from the Autworks database to interrogate 1 million chemical/gene interactions in the comparative toxicogenomics database. Any bias towards ASG's was statistically determined for each chemical. Many suspect compounds identified in epidemiology, including tetrachlorodibenzodioxin, pesticides, particulate matter, benzo(a)pyrene, heavy metals, valproate, acetaminophen, SSRI's, cocaine, bisphenol A, phthalates, polyhalogenated biphenyls, flame retardants, diesel constituents, terbutaline and oxytocin, inter alia showed a significant degree of bias towards ASG's, as did relevant endogenous agents (retinoids, sex steroids, thyroxine, melatonin, folate, dopamine, serotonin). Numerous other suspected endocrine disruptors (over 100) selectively targeted ASG's including paraquat, atrazine and other pesticides not yet studied in autism and many compounds used in food, cosmetics or household products, including tretinoin, soy phytoestrogens, aspartame, titanium dioxide and sodium fluoride. Autism polymorphisms influence the sensitivity to some of these chemicals and these same genes play an important role in barrier function and control of respiratory cilia sweeping particulate matter from the airways. Pesticides, heavy metals and pollutants also disrupt barrier and/or ciliary function, which is regulated by sex steroids and by bitter/sweet taste receptors. Further epidemiological studies and neurodevelopmental and behavioural research is warranted to determine the relevance of large number of

suspect candidates whose addition to the environment, household, food and cosmetics might be fuelling the autism epidemic in a gene-dependent manner.

hero.3479559

Chen, JH, ui; Su, Y, anHua; Peng, X, ueQi; Zhao, B, in; Yu, XS; Cheng, Q, iJun; Huang, ZX; Shi, MM; Liu, H, uiFen; Ke, X, iaYi; Chen, J; Zhao, B, enHua; Inc, DP. (2016). Association between Prenatal Phthalate Exposure and Birth Outcomes. 1-10.

Objective: To understand the association between exposure in pregnant women to phthalic acid esters (PAEs) and birth outcomes. Method: The study was conducted from April to June 2013 in Xiamen, China. A total 1020 pregnant women (gestational age <= 16 weeks) met the inclusion criteria and were included in the cohort. Finally, 25 women with premature delivery and 15 with low birth weight were defined as case groups. According to the study criteria, we selected 100 healthy participants as a control group. Participant information was collected by questionnaires and urine samples were collected, and detect five PAEs (MMP, MEP, MBP, MBzP, and MEHP) levels in urine samples. Single and multi-factor logistic analyses were used to analyze the association between PAE concentration and birth outcomes. Results: Medians of the five PAEs above in the premature delivery group were 36.13 ng/ml, 19.02 ng/ml, 13.64 ng/ml, 2.11 ng/ml, 43.47 ng/ml, respectively. In the control group, these were 35.48 ng/ml, 17.62 ng/ml, 10.15 ng/ml, 2.34 ng/ml, 35.62 ng/ml, respectively. The result of multi-factor logistic analysis indicated that MBP and MEHP were associated with premature delivery: OR 1.629, 95% CI (1.067, 2.488), OR 1.675, 95% CI (1.028, 2.729), respectively. Medians of the five PAEs in the low birth weight group were 37.28 ng/ml, 21.36 ng/ml, 14.60 ng/ml, 2.63 ng/ml, 45.72 ng/ml, respectively. In the control group, these were 35.48 ng/ml, 17.62 ng/ml, 10.15 ng/ml, 2.34 ng/ml, 35.62 ng/ml respectively. MEP, MBP, and MEHP were associated with low birth weight: OR 1.699, 95% CI (1.074, 2.688), OR 1.621, 95% CI (1.061, 2.475), and OR 1.817, 95% CI (1.005, 3.284), respectively. Conclusion: MBP and MEHP exposure in pregnant women were risk factors of premature delivery and MEP, MBP, MEHP exposure were risk factors of low birth weight. Preventing or reducing environmental exposure of pregnant women to these PAEs is of utmost importance.

hero.3350199

Cheng, Z; Li, HH; Wang, HS; Zhu, XM; Sthiannopkao, S; Kim, KW; Yasin, MS; Hashim, JH; Wong, MH. (2016). Dietary exposure and human risk assessment of phthalate esters based on total diet study in Cambodia. Environ Res 150: 423-430. http://dx.doi.org/10.1016/j.envres.2016.06.011.

Phthalate esters are used in a wide variety of consumer products, and human exposure to this class of compounds is widespread. Nevertheless, studies on dietary exposure of human to phthalates are limited. In this study, to assess the daily intakes of phthalate esters and the possible adverse health impacts, different food samples were collected from three areas of Cambodia, one of the poorest countries in the world. The phthalate ester concentrations in Kampong Cham, Kratie and Kandal provinces ranged from 0.05 to 2.34 (median 0.88) μgg(-1), 0.19-1.65 (median 0.86) μgg(-1) and 0.24-3.05 (median 0.59) μgg(-1) wet weight (ww), respectively. Di-2-Ethylhexyl phthalate (DEHP) and diisobutyl phthalate (DiBP) were the predominant compounds among all foodstuffs. The estimated daily intake (EDI) of phthalate esters for the general population in Kampong Cham, Kratie and Kandal was 34.3, 35.6 and 35.8μgkg(-1) bw d(-1), respectively. The dietary daily intake of DEHP, benzylbutyl phthalate (BBP) and di-n-butyl phthalate (DBP) in Kampong Cham, Kratie and Kandal were below the tolerable daily intakes (TDI) imposed by the European Food Safety Authority (EFSA) and reference doses (RfD) imposed by The United States Environmental Protection Agency (USEPA). Rice contributed the greatest quantity of DEHP to the daily intake in Cambodia so may deserve further exploration. To our knowledge, this is the first study to investigate the occurrence and the daily intakes of phthalate esters in Cambodia.

hero.3464593

Cheon, KY; Kil, K, iH; Choi, JI, n; Kim, R, aYon; Kim, M, eeRan; Kim, JH; Cho, HH, ee. (2016). Parenteral Exposure to DEHP and Its Effect on the Microstructure of Bone and Wnt Signaling Pathway in F2 Female Mice. BioChip Journal 10: 233-240. http://dx.doi.org/10.1007/s13206-016-0309-2.

Diethylhexyl phthalate (DEHP) is a widely used plasticizer, and its exposure via the enteral and parenteral routes can affect estrogen function and has transgenerational effect. The bones are the most important target organs for estrogen; however, the related gene pathway and the effects of DEHP on bones remain

unknown. In this study, we evaluated whether parenteral exposure to DEHP has effects on bone microarchitecture in F2 mice, and determined the related gene pathway.

Pregnant mice (F0) were exposed to DEHP, at doses of 30 mu g/kg/day (low dose) and 400 mu g/kg/day (high dose), and corn oil during pregnancy and lactation. F2 siblings were not treated with DEHP. We performed micro-CT to analyze the microstructure of the tibial head and microarray analysis on ovary cells from F2 female siblings of 17-18 weeks of age to evaluate the gene expression.

The percentage of bone volume in the low- (5.55% +/- 0.85%) and high-dose (7.09% +/- 4.15%) groups was higher than that in the control (2.25% +/- 1.22%; P < 0.05). Trabecular number (per mm(2)) was higher in the low- (0.87 +/- 0.12) and high-dose (0.95 +/- 0.55) groups compared to that in the control (0.37 +/- 0.21; P<0.05). Trabecular thickness was greater in the high-dose group (0.073 +/- 0.006 mu m) than in the control (0.060 +/- 0.002 pm) and low-dose (0.063 +/- 0.004 mu m) groups. The structure model index (SMI) of the low- and high-dose groups was significantly lower than the corresponding value in the control group (P<0.05). Micro-CT analysis indicated proliferative changes in trabectlar bone in the treated F2 siblings. In the microarray analysis of ovary cells, CTNNB2 (catenin beta 1) and PPP3R1 gene expressions were significantly modified in the low- and high-dose groups. SFRPI, DVL2, WNT11, and WNT16 showed significant expression changes in the low-dose group, but not in the high-dose group. Taken together, parenteral exposure to DEHP during pregnancy and lactation could influence the trabecular bone microarchitectures of F2 siblings and affect certain genes associated with the Wnt signaling pathway.

hero.3207434

Choi, H; Schmidbauer, N; Bornehag, CG. (2016). Non-microbial sources of microbial volatile organic compounds. Environ Res 148: 127-136. http://dx.doi.org/10.1016/j.envres.2016.03.026.
BACKGROUND: The question regarding the true sources of the purported microbial volatile organic compounds (MVOCs) remains unanswered.

OBJECTIVE: To identify microbial, as well as non-microbial sources of 28 compounds, which are commonly accepted as microbial VOCs (i.e. primary outcome of interest is Σ 28 VOCs).

METHODS: In a cross-sectional investigation of 390 homes, six building inspectors assessed water/mold damage, took air and dust samples, and measured environmental conditions (i.e., absolute humidity (AH, g/m(3)), temperature (C), ventilation rate (ACH)). The air sample was analyzed for volatile organic compounds (µg/m(3)) and; dust samples were analyzed for total viable fungal concentration (CFU/g) and six phthalates (mg/g dust). Four benchmark variables of the underlying sources were defined as highest quartile categories of: 1) the total concentration of 17 propylene glycol and propylene glycol ethers (Σ17 PGEs) in the air sample; 2) 2,2,4-trimethyl-1,3-pentanediol monoisobutyrate (TMPD-MIB) in the air sample; 3) semi-quantitative mold index; and 4) total fungal load (CFU/g).

RESULTS: Within severely damp homes, co-occurrence of the highest quartile concentration of either Σ17 PGEs or TMPD-MIB were respectively associated with a significantly higher median concentration of Σ 28 VOCs (8.05 and 13.38µg/m(3), respectively) compared to the reference homes (4.30 and 4.86µg/m(3), respectively, both Ps 0.002). Furthermore, the homes within the highest quartile range for Σ fungal load as well as AH were associated with a significantly increased median Σ 28 VOCs compared to the reference group (8.74 vs. 4.32µg/m(3), P=0.001). Within the final model of multiple indoor sources on Σ 28 VOCs, one natural log-unit increase in summed concentration of Σ17 PGEs, plus TMPD-MIB (Σ 17 PGEs + TMPD-MIB) was associated with 1.8-times (95% CI, 1.3-2.5), greater likelihood of having a highest quartile of Σ 28 VOCs, after adjusting for absolute humidity, history of repainting at least one room, ventilation rate, and mold index (P-value =0.001). Homes deemed severely mold damaged (i.e., mold index =1) were associated with 1.7-times (95% CI, 0.8-3.6), greater likelihood of having a highest quartile of Σ 28 VOCs, even though such likelihood was not significant (P-value =0.164). In addition, absolute humidity appeared to positively interact with mold index to significantly elevate the prevalence of the highest quartile category of Σ 28 VOCs.

CONCLUSION: The indoor concentration of Σ 28 VOCs, which are widely accepted as MVOCs, are significantly associated with the markers of synthetic (i.e. Σ17 PGEs and TMPD-MIB), and to less extent, microbial (i.e., mold index) sources.

hero.3469260

Choi, W; Kim, S; Baek, YW; Choi, K; Lee, K; Kim, S; Yu, SD; Choi, K. (2016). Exposure to environmental chemicals among Korean adults-updates from the second Korean National Environmental Health Survey (2012-2014). Int J Hyg

Environ Health. http://dx.doi.org/10.1016/j.ijheh.2016.10.002.
National biomonitoring program can offer solid scientific evidence on exposure profiles of environmental chemicals at a national level, and provide a snapshot of changing exposure level over time. Therefore, several countries have maintained such programs for developing environmental health policies. The Korean National Environmental Health Survey (KoNEHS) was designed to understand the level of human exposure to environmental chemicals by time and location, and to identify possible sources of such exposure. The 2nd stage of KoNEHS, which was conducted between 2012 and 2014, examined a total of 6478 adult subjects over 19 years of age, and measured 21 environmental chemicals of major policy concern. Compared to the findings from the first stage monitoring (2009-2011), slightly higher levels of blood lead were observed, while those of mercury remained similar. Blood metal concentrations, however, were higher than those reported from national biomonitoring programs of United States, Germany and Canada. The urinary concentrations of phthalates metabolites were lower, but those of t,t-muconic acid and BPA were higher than those reported in the first stage survey. The urinary cotinine level decreased perhaps reflecting general declining patterns of first- and second-hand smoking. The results of the second stage survey were made available for public use since April 2016. Some policy efforts appear to be at least in part effective on mitigating chemical exposure among people, e.g., urinary phthalate metabolites and cotinine, while further confirmations are warranted. In-depth assessments will be conducted to identify vulnerable groups and important exposure pathways.

hero.3469406

Corbasson, I; Hankinson, SE; Stanek, EJ; Reeves, KW. (2016). Urinary bisphenol-A, phthalate metabolites and body composition in US adults, NHANES 1999-2006. Int J Environ Health Res 26: 606-617. http://dx.doi.org/10.1080/09603123.2016.1233524.
BACKGROUND: Exposure to bisphenol-A (BPA) and phthalates is highly prevalent. Prior studies have not assessed associations between urinary levels of BPA and phthalate metabolites and body composition.

METHODS: National Health and Nutrition Examination Survey (NHANES) data from 1999 to 2006 on adults aged 20 were analyzed by linear regression for associations between urinary BPA, monoethyl phthalate, monobutyl phthalate (MBP), monoethylhexyl phthalate (MEHP), and monobenzyl phthalate (MBzP) and lean mass, fat mass, and percent body fat.

RESULTS: BPA and phthalate metabolites were not independently associated with fat mass or percent body fat. Significant inverse associations were observed with lean mass, with the strongest association observed for BPA in men (mean lean mass 1.39kg lower for quartile 4 vs. quartile 1, p trend=0.02).

CONCLUSIONS: BPA and some phthalates could have important, negative effects on muscle and may affect conditions related to deficits in lean mass, though additional research is needed.

hero.3469557

D'alessandro, A; Nemkov, T; Hansen, KC. (2016). Rapid detection of DEHP in packed red blood cells stored under European and US standard conditions. Blood Transfus 14: 140-144. http://dx.doi.org/10.2450/2015.0210-15.

hero.3479547

de Barros, AL; Rosa, JL; Cavariani, MM; Borges, CS; Villela e Silva, P; Bae, JH; Anselmo-Franci, JA; Cristina Arena, A. (2016). In utero and lactational exposure to fipronil in female rats: Pregnancy outcomes and sexual development. J Toxicol Environ Health A 79: 266-273. http://dx.doi.org/10.1080/15287394.2016.1149132.
Fipronil, a phenylpyrazole insecticide, is used in agriculture, veterinary medicine, and public health. Because this insecticide is considered a potential endocrine disruptor, the aim of this study was to examine the influence of perinatal exposure to fipronil on neonatal female reproductive system development. Pregnant rats were exposed (via gavage) daily to fipronil (0.03, 0.3, or 3 mg/kg) from gestational day 15 to day 7 after birth, and effects on the reproductive functions assessed on postnatal day (PND) 22. No signs of maternal toxicity were observed during daily treatment with fipronil. Perinatal exposure to the highest dose of fipronil (3 mg/kg) delayed the age of vaginal opening (VO) and first estrus without markedly affecting the anogenital distance (AGD). Further, exposure to 0.3 mg/kg fipronil produced a significantly shorter estrus cycle and reduced number of cycles during the period of evaluation. However, the other reproductive parameters analyzed, including fertility, hormone levels, sexual behavior, and histology of ovaries and uterus, displayed

no marked alterations. In this experimental model, fipronil interfered with development of neonatal female reproductive system as evidenced by delay in VO and estrus cycle alterations without apparent significant effects on fertility. Further studies are needed to identify the mechanisms of action associated with the observed female reproductive system changes.

hero.3350366

DeBartolo, D; Jayatilaka, S; Yan Siu, N; Rose, M; Ramos, RL; Betz, AJ. (2016). Perinatal exposure to benzyl butyl phthalate induces alterations in neuronal development/maturation protein expression, estrogen responses, and fear conditioning in rodents. Behav Pharmacol 27: 77-82. http://dx.doi.org/10.1097/FBP.0000000000000190.

Phthalate exposure has recently been associated with behavioral actions that are linked to its endocrine-disrupting properties. The purpose of this study was to investigate the molecular, anatomical, and behavioral effects of indirect perinatal benzyl butyl phthalate (BBP) exposure in offspring of BBP-treated pregnant dams. In two separate experiments, we administered BBP (10.0 µg/ml) on food pellets to pregnant dams and examined the offspring. The first experiment revealed reproductive anatomical abnormalities linked to BBP's endocrine-disrupting properties, whereas histological analysis revealed preserved hippocampal neuronal migration. The second experiment demonstrated learning and memory impairments accompanied by molecular abnormalities in multiple brain regions. Offspring from BBP-treated dams had altered levels of several proteins important for neuronal circuitry formation, tissue development, and maturation. We suggest that BBP administration disrupts normal learning and that these effects could be related to alterations in brain development and result in a phenotype similar to that observed in neurodevelopmental disorders.

hero.3479518

Degrelle, S; Chissey, A; Shoaito, H; Gil, S; Fournier, T. (2016). IMPACT OF MONO-2-ETHYLHEXYL PHTHALATE (MEHP) EXPOSURE ON PPAR gamma EXPRESSION AND ACTIVITY DURING HUMAN CYTOTROPHOBLAST DIFFERENTIATION. Placenta 45: 96-96.

hero.3479505 REVIEW

Del Pup, L; Mantovani, A; Cavaliere, C; Facchini, G; Luce, A; Sperlongano, P; Caraglia, M; Berretta, M. (2016). Carcinogenetic mechanisms of endocrine disruptors in female cancers (Review). Oncol Rep 36: 603-612. http://dx.doi.org/10.3892/or.2016.4886.

Endocrine disruptors (EDs) are pollutants that alter the endocrine system and are involved in carcinogenesis. EDs have multiple and complex levels of action. They can affect the synthesis, release and transport of natural hormones. In target tissues, EDs can reduce or increase the effects of natural hormones on their receptors and change signaling cascades. When ED exposure happens at critical periods of life, from embryo to puberty, they can act at doses considered safe for an adult. Furthermore, their epigenetic effects can also influence the cancer risk of future generations. The cancer mechanisms of known EDs are hereby reviewed, There are thousands of newly introduced substances whose potential endocrine-disrupting and cancer effects are completely unknown. Although there are still gaps in our knowledge, these data support the urgent need for health and environmental policies aimed at protecting the public and in particular, the developing fetus and women of reproductive age.

hero.3469196

Dempsey, JL; Cui, JY. (2017). Long Non-Coding RNAs: A Novel Paradigm for Toxicology. Toxicol Sci 155: 3-21. http://dx.doi.org/10.1093/toxsci/kfw203.

Long non-coding RNAs (lncRNAs) are over 200 nucleotides in length and are transcribed from the mammalian genome in a tissue-specific and developmentally regulated pattern. There is growing recognition that lncRNAs are novel biomarkers and/or key regulators of toxicological responses in humans and animal models. Lacking protein-coding capacity, the numerous types of lncRNAs possess a myriad of transcriptional regulatory functions that include cis and trans gene expression, transcription factor activity, chromatin remodeling, imprinting, and enhancer up-regulation. LncRNAs also influence mRNA processing, post-transcriptional regulation, and protein trafficking. Dysregulation of lncRNAs has been implicated in various human health outcomes such as various cancers, Alzheimer's disease, cardiovascular disease, autoimmune diseases, as well as intermediary metabolism such as glucose, lipid, and bile acid homeostasis.

Interestingly, emerging evidence in the literature over the past five years has shown that lncRNA regulation is impacted by exposures to various chemicals such as polycyclic aromatic hydrocarbons, benzene, cadmium, chlorpyrifos-methyl, bisphenol A, phthalates, phenols, and bile acids. Recent technological advancements, including next-generation sequencing technologies and novel computational algorithms, have enabled the profiling and functional characterizations of lncRNAs on a genomic scale. In this review, we summarize the biogenesis and general biological functions of lncRNAs, highlight the important roles of lncRNAs in human diseases and especially during the toxicological responses to various xenobiotics, evaluate current methods for identifying aberrant lncRNA expression and molecular target interactions, and discuss the potential to implement these tools to address fundamental questions in toxicology.

hero.3466593

Dereumeaux, C; Fillol, C; Charles, MA; Denys, S. (2016). The French human biomonitoring program: First lessons from the perinatal component and future needs. Int J Hyg Environ Health. http://dx.doi.org/10.1016/j.ijheh.2016.11.005.

This paper presents a progress report of the French human biomonitoring (HBM) program established in 2010. This program has been designed to provide a national representative estimation of the French population's exposure to various environmental chemicals and to study the determinants of exposure. This program currently consists in two surveys: a perinatal component related to a selection of 4145 pregnant women who have been enrolled in the Elfe cohort (the French Longitudinal Study since Childhood) in 2011, and a general population survey related to adults aged 18-74 years and children as from 6 years (Esteban). The aim of this manuscript is to present highlights of the French human biomonitoring program with particular focus on the prioritization of biomarkers to be analyzed in the program and the selection of biomarkers applied to both program components. The Delphi method was used to establish a consensual list of prioritized biomarkers in 2011. First results of the perinatal component of the French HBM program have shown that the biomarkers prioritized were relevant, as almost all pregnant women were exposed to them. However, for some biomarkers, levels' decreases have been observed which may partly be explained by measures taken to prohibit some of these chemicals (e.g. atrazine) and by industrial processes evolutions leading to the substitution of others (e.g. bisphenol A, di-2-ethylhexyl phthalate/DEHP, dialkyl phosphates). Therefore, the list of biomarkers to be monitored in the French HBM program has been implemented to include some substitutes of biomarkers prioritized in the first instance (e.g. bisphenol S, F). Finally, this method combines rigor and flexibility and helped us to build a prioritized list that will be shared and supported by many if not all actors.

hero.3469298

Dereumeaux, C; Saoudi, A; Pecheux, M; Berat, B; de Crouy-Chanel, P; Zaros, C; Brunel, S; Delamaire, C; le Tertre, A; Lefranc, A; Vandentorren, S; Guldner, L. (2016). Biomarkers of exposure to environmental contaminants in French pregnant women from the Elfe cohort in 2011. Environ Int 97: 56-67. http://dx.doi.org/10.1016/j.envint.2016.10.013.

BACKGROUND: As part of the perinatal component of the French Human Biomonitoring (HBM) program, biomarkers levels of various chemicals have been described among pregnant women having given birth in continental France in 2011 and who have been enrolled in the Elfe cohort (French Longitudinal Study since Childhood). This paper describes the design of the study and provides main descriptive results regarding exposure biomarkers levels.

METHODS: Exposure biomarkers were measured in biological samples collected at delivery from pregnant women randomly selected among the participants in the clinical and biological component of the Elfe cohort (n=4145). The geometric mean and percentiles of the levels distribution were estimated for each biomarker. The sampling design was taken into account in order to obtain estimates representative of the French pregnant women in 2011.

RESULTS: Results provide a nation-wide representative description of biomarker levels for important environmental contaminants among pregnant women who gave birth in France in 2011. Bisphenol A (BPA), and some metabolites of phthalates, pesticides (mainly pyrethroids), dioxins, furans, polychlorobiphenyls (PCBs), brominated flame retardants (BFRs), perfluorinated compounds (PFCs) and metals (except uranium) were quantified in almost 100% of the pregnant women. Some compounds showed a downward trend compared to previous studies (lead, mercury), but others did not (pyrethroids) and should be further monitored.

/>CONCLUSION AND PERSPECTIVES: The present results show that French pregnant women are exposed to a wide variety of pollutants, including some that have been banned or restricted in France.

hero.3469472

Dobrzyńska, MM. (2016). Phthalates - widespread occurrence and the effect on male gametes. Part 2. The effects of phthalates on male gametes and on the offspring. Rocz Panstw Zakl Hig 67: 209-221.
UNLABELLED: The general exposure to endocrine disruptors, including phthalates, is considered as one of the reason diminished sperm count and deteriorated sperm quality, which may lead to infertility and higher incidence of congenital malformations of the genital tract. This article describes the effects of selected phthalates di(2-ethylhexyl)phthalate (DEHP), dibutyl phthalate (DBP); butylbenzyl phthalate (BBP), diethyl phthalate (DEP), di-isononyl phthalate (DINP) on the male gametes, reproduction and the offspring of exposed animals. Results of several papers in vitro showed that above mentioned phthalates are weakly estrogenic, whereas in vivo studies showed that they have rather antiandrogenic abilities. Review of papers regarding to laboratory animals confirmed that phthalates cause diminished sperm count, increased frequency of abnormal spermatozoa and DNA damage in germ cells, especially after chronic exposure and in case exposure of immature animals. Phthalates may induce in male gametes mutations leading to increased pre- and postnatal mortality of the offspring and to incidence of congenital malformations, growth retardation, delay in sexual development, shortening of anogenital distance in males, disturbances in sex ratio and diminished quality of semen in F1 generation. The sensitivity on mammalian life stages on phthalates seems to be as follows: fetal > peripubertal > adult. The human studies provided limited evidence of an association between phthalate exposure and semen quality. Concentration of phthalates in semen of men at the level from 0.08 to 1.32 mg/kg was related to declined semen quality and infertility. Majority of human data showed the connection of increased level of phthalates in urine and sperm quality, however on the basis results of other studies, the impact of environmental exposure on sperm parameters seems to be rather small.

KEY WORDS: phthalates, sperm count and quality, pre- and perinatal exposure, mammalian and human effects.

hero.3469358

Doherty, BT; Engel, SM; Buckley, JP; Silva, MJ; Calafat, AM; Wolff, MS. (2017). Prenatal phthalate biomarker concentrations and performance on the Bayley Scales of Infant Development-II in a population of young urban children. Environ Res 152: 51-58. http://dx.doi.org/10.1016/j.envres.2016.09.021.
INTRODUCTION: Evidence suggests prenatal phthalate exposures may have neurodevelopmental consequences. Our objective was to investigate prenatal exposure to phthalates and cognitive development in a cohort of young urban children.

MATERIALS AND METHODS: We recruited pregnant women in New York City from 1998 to 2002 and measured concentrations of nine phthalate metabolites in urine collected in late pregnancy. We administered a neurodevelopmental screening instrument, the Bayley Scales of Infant Development II (BSID-II), to children who returned for follow-up at approximately 24 months (n=276). We estimated associations between phthalate metabolite concentrations in maternal urine and BSID-II indices (Mental Development Index (MDI), Psychomotor Development Index (PDI)).

RESULTS: We observed no associations between phthalate metabolite concentrations and performance on the MDI or PDI in boys and girls combined. We did, however, observe evidence of effect measure modification by sex. We observed several negative associations between metabolite concentrations and both MDI and PDI scores among girls, suggesting poorer performance across multiple metabolites, with estimates equal to a 2-3 point decrease in score per ln-unit increase in creatinine-standardized metabolite concentration. Conversely, we observed multiple weakly positive associations among boys, equal to a 1-2 point increase in score per ln-unit increase in metabolite concentration. The strongest associations were for the metabolites mono-n-butyl phthalate, mono-isobutyl phthalate, monobenzyl phthalate, and mono(3-carboxylpropyl) phthalate (MCPP).

CONCLUSIONS: Girls of mothers with higher urinary concentrations of MCPP and metabolites of dibutyl phthalates had lower MDI scores on the BSID-II. These same biomarker concentrations were often associated with improved scores among boys. We observed similar results for MnBP, MCPP, and MBzP on the PDI. Given the prevalence of phthalate exposures in reproductive aged women, the implications of potential neurotoxicity warrant further investigation.

hero.3466560

Dong, X; Dong, J; Zhao, Y; Guo, J; Wang, Z; Liu, M; Zhang, Y; Na, X. (2017). Effects of Long-Term In Vivo Exposure to Di-2-Ethylhexylphthalate on Thyroid Hormones and the TSH/TSHR Signaling Pathways in Wistar Rats. Int J Environ Res Public Health 14. http://dx.doi.org/10.3390/ijerph14010044.

Di-(2-ethylhexyl)phthalate (DEHP) was a widely used chemical with human toxicity. Recent in vivo and in vitro studies suggested that DEHP-exposure may be associated with altered serum thyroid hormones (THs) levels, but the underlying molecular mechanisms were largely unknown. To explore the possible molecular mechanisms, 128 Wistar rats were dosed with DEHP by gavage at 0, 150, 300, and 600 mg/kg/day for 3 months (M) and 6 M, respectively. After exposure, expression of genes and proteins in the thyroid, pituitary, and hypothalamus tissues of rats were analyzed by Q-PCR and western blot, while the sera and urine samples were assayed by radioimmunoassay and ELISA. Results showed that serum THs levels were suppressed by DEHP on the whole. DEHP treatment influenced the levels of rats' thyrotropin releasing hormone receptor (TRHr), Deiodinases 1 (D1), thyroid stimulating hormone beta (TSHβ), sodium iodide symporter (NIS), thyroid stimulating hormone receptor (TSHr), thyroperoxidase (TPO), thyroid transcription factor 1 (TTF-1), and thyroglobulin (TG) mRNA/protein expression in the hypothalamus-pituitary-thyroid (HPT) axis and decreased urine iodine. Taken together, observed findings indicate that DEHP could reduce thyroid hormones via disturbing the HPT axis, and the activated TSH/TSHR pathway is required to regulate thyroid function via altering TRHr, TSHβ, NIS, TSHr, TPO, TTF-1 and TG mRNA/protein expression of the HPT axis.

hero.3479551

Du, J; Gao, R; Mu, H, ui. (2016). A Novel Molecularly Imprinted Polymer Based on Carbon Nanotubes for Selective Determination of Dioctyl Phthalate from Beverage Samples Coupled with GC/MS. Food Analytical Methods 9: 2026-2035. http://dx.doi.org/10.1007/s12161-015-0383-4.

Phthalates represent a potential risk for humans, since they are ubiquitous environmental contaminants. Efficient extraction and purification procedures are demanded for the detection of low concentration levels of phthalates. In this work, a novel type of molecularly imprinted polymers coated onto the surface of vinyl functionalized multi-walled carbon nanotubes was synthesized and coupled with gas chromatography-mass spectrometry (GC/MS) for the selective separation and determination of dioctyl phthalate (DOP) in beverage samples. The morphology, structure property, and thermostability of the resultant polymers were characterized by transmission electron microscopy, Fourier transform infrared spectroscopy, and thermogravimetric analysis. The adsorption properties of the prepared polymers were investigated by equilibrium rebinding and competitive experiments. The resultant imprinted nanomaterials exhibited high capacity and favorable selectivity. In addition, the feasibility of the developed method using the obtained imprinted polymers as a solid-phase sorbent coupled with GC/MS for the selective isolation and determination of DOP in different beverage samples was demonstrated. Under optimal conditions, the limit of detection of the proposed method for DOP was 2.3 ng L-1. DOP spiked at three levels of concentration in beverage samples was extracted and determined through the application of the present method, with recoveries ranging from 88.6 to 93.0 % with relative standard deviations less than 5.6 %.

hero.3469308

Estors Sastre, B; Bragagnini Rodríguez, P; Fernández Atuan, R; Delgado Alvira, R; Rihuete Heras, MA; Gracia Romero, J. (2015). [Endocrine disrupting chemicals exposure and other parental factors in hypospadias and cryptorchidism etiology]. Cir Pediatr 28: 128-132.

AIM OF THE STUDY: To investigate the association between endocrine disrupting chemicals (EDC) exposure and other paternal factors in the etiology of hipospadias and cryptorchidism.

METHODS: A case-control study. Cases were infants between 0 and 6 years of age diagnosed with hypospadias or cryptorchidism in our pediatric urology and general pediatric surgery services during a period of 6 months, and controls were infants with the same range of age attending the same services without any urological problem. Several variables were collected by face-to-face interviews with both parents. After data abstraction, we compared the characteristics of both groups using parametric statistical tests.

MAIN RESULTS: A total of 180 patients were studied, 90 cases (45 hypospadias/45 cryptorchidism) and 90 controls with a mean age of 2,37 1.50 years [range 0,5-6].

Median of mothers age was significantly greater in case group (34,40 5,64 versus 31,74 5,05; p= 0,001). Significant differences were observed between cases and controls in regard to maternal occupational exposure to EDC (mainly phthalates), adjusted Odds ratio (OR) was 3.67 [95% confidence interval (CI): 1.28-10.51; p= 0,018] and regarding the paternal occupational exposure to EDC (mainly pesticides and herbicides), adjusted OR was 6.65 [95% CI: 2.60-17.02; p= 0,001]. Increased risk was also observed in smoking fathers and fathers who drink alcohol, adjusted Odds ratio were 2.36 [95% CI: 1.11.

CONCLUSIONS: This study represents a little contribution to the possible etiologic factors of hypospadias and cryptorchidism, further studies with higher statistical power would be needed to prove it.

hero.3479497

Euling, S; Androulakis, I; Benson, B; Chiu, W; Foster, P. (2009). Approach to using toxicogenomic data in U.S. EPA human health risk assessments: A dibutyl phthalate case study. Gov Rep Announce Index.
Prepared in cooperation with University of Medicine and Dentistry of New Jersey, Newark., National Inst. of Environmental Health Sciences, Research Triangle Park, NC. and Food and Drug Administration, Rockville, MD. We developed a systematic approach for evaluating and utilizing toxicogenomic data in health assessment. This report describes this approach and a case study conducted for dibutyl phthalate (DBP) to illustrate the approach. As a result of the case-study exercise, we refined the initial case-study approach for general use in new chemical assessments. In this report, we reviewed some of the recent and ongoing activities regarding the use of genomic data in risk assessment, inside and outside of the U.S. Environmental Protection Agency (EPA). We also identified research needs, recommendations, and issues for future consideration when using genomic data in risk assessments. Toxicogenomics is the application of genomic technologies (e.g., transcriptomics, proteomics, metabolomics, genome sequence analysis) to study the effects of environmental chemicals on human health and the environment.

hero.3479558

Ferguson, KK; Cantonwine, DE; Mcelrath, TF; Mukherjee, B; Meeker, JD. (2016). Repeated measures analysis of associations between urinary bisphenol-A concentrations and biomarkers of inflammation and oxidative stress in pregnancy. Reprod Toxicol 66: 93-98. http://dx.doi.org/10.1016/j.reprotox.2016.10.002.
Bisphenol-A (BPA) exposure occurs commonly and may adversely impact pregnancy. Endocrine disruption is posited as the primary mechanism of action, but oxidative stress and inflammation pathways may also be important. We investigated associations between BPA exposure and oxidative stress and inflammation in 482 pregnant women. Participants were recruited early in pregnancy and provided urine and plasma at up to four visits. We measured total BPA and two biomarkers of oxidative stress (8-hydroxydeoxyguanosine and 8-isoprostane) in urine from each visit. Inflammation markers, including C-reactive protein and four cytokines were measured in plasma from the same time points. In adjusted models, an interquartile range increase in BPA was associated with significant increases in both oxidative stress biomarkers (5-9% increase). Additionally, we observed significantly higher IL-6 concentrations in association with an interquartile range increase in BPA (8.95% increase). These systemic changes consequent to BPA exposure may mediate adverse birth outcomes and/or fetal development.

hero.3350207

Ferguson, KK; Chen, YH; Vanderweele, TJ; Mcelrath, TF; Meeker, JD; Mukherjee, B. (2016). Mediation of the Relationship between Maternal Phthalate Exposure and Preterm Birth by Oxidative Stress with Repeated Measurements across Pregnancy. Environ Health Perspect. http://dx.doi.org/10.1289/EHP282.
BACKGROUND: Mediation analysis is useful for understanding mechanisms and has been utilized minimally in the study of the environment and disease.

OBJECTIVE: We examined mediation of the association between phthalate exposure during pregnancy and preterm birth by oxidative stress.

METHODS: This nested case-control study of preterm birth (N=130 cases, 352 controls) included women who delivered in Boston from 2006-2008. Phthalate metabolites and 8-isoprostane, an oxidative stress biomarker, were measured in urine from three visits in pregnancy. We applied four counterfactual mediation methods: Method 1) utilizing exposure and mediator averages; Method 2) using averages but allowing for an exposure-mediator interaction; Method 3) incorporating longitudinal measurements of the exposure and mediator; and Method 4) using longitudinal

measurements and allowing for an exposure-mediator interaction.

RESULTS: We observed mediation of the associations between phthalate metabolites and all preterm birth by 8-isoprostane, with the greatest estimated proportion mediated observed for spontaneous preterm births specifically. Fully utilizing repeated measures of the exposure and mediator improved precision of indirect (i.e., mediated) effect estimates, and including an exposure-mediator interaction increased the estimated proportion mediated. For example, for mono-2-ethyl-carboxy-propyl phthalate (MECPP), a metabolite of di-2-ethylhexyl phthalate (DEHP), the percent of the total effect mediated by 8-isoprostane increased from 47% to 60% with inclusion of an exposure-mediator interaction term, in reference to a total adjusted odds ratio of 1.67 or 1.48, respectively.

CONCLUSIONS: This demonstrates mediation of the phthalate-preterm relationship by oxidative stress, and the utility of complex regression models in capturing mediated associations when repeated measures of exposure and mediator are available and an exposure-mediator interaction may exist.

hero.3380523

Ferguson, KK; Meeker, JD. (2016). The Role of Environmental Exposures in Preterm Birth. In Molecular and Integrative Toxicology. http://dx.doi.org/10.1007/978-3-319-27449-2_9.

Preterm birth is a significant yet poorly understood public health problem that may arise in part from maternal exposure to chemicals in the environment. This review explores the state of the knowledge on prematurity in relation to: (1) Organic pollutants, including persistent organic pollutants, such as dichlorodiphenyltrichloroethane, polychlorinated biphenyls, and perfluorinated compounds, disinfection byproducts, such as trihalomethanes, non-persistent pesticides, such as atrazine, and non-persistent organics of emerging concern, such as phthalates and bisphenol-A; (2) Metals and metalloids, including lead, cadmium, arsenic, and mercury; and (3) Air pollutants, including EPA criteria air contaminants, environmental tobacco smoke, and polycyclic aromatic hydrocarbons. We also highlight pervasive study limitations as well as important directions for future research.

hero.3350218

Ferguson, KK; Meeker, JD; Cantonwine, DE; Chen, YH; Mukherjee, B; Mcelrath, TF. (2016). Urinary phthalate metabolite and bisphenol A associations with ultrasound and delivery indices of fetal growth. Environ Int 94: 531-537. http://dx.doi.org/10.1016/j.envint.2016.06.013.

Growth of the fetus is highly sensitive to environmental perturbations, and disruption can lead to problems in pregnancy as well as later in life. This study investigates the relationship between maternal exposure to common plasticizers in pregnancy and fetal growth. Participants from a longitudinal birth cohort in Boston were recruited early in gestation and followed until delivery. Urine samples were collected at up to four time points and analyzed for concentrations of phthalate metabolites and bisphenol A (BPA). Ultrasound scans were performed at four time points during pregnancy for estimation of growth parameters, and birthweight was recorded at delivery. Growth measures were standardized to a larger population. For the present analysis we examined cross-sectional and repeated measures associations between exposure biomarkers and growth estimates in 482 non-anomalous singleton pregnancies. Cross-sectional associations between urinary phthalate metabolites or BPA and growth indices were imprecise. However, in repeated measures models, we observed significant inverse associations between di-2-ethylhexyl phthalate (DEHP) metabolites and estimated or actual fetal weight. An interquartile range increase in summed DEHP metabolites was associated with a 0.13 standard deviation decrease in estimated or actual fetal weight (95% confidence interval=-0.23, -0.03). Associations were consistent across different growth parameters (e.g., head circumference, femur length), and by fetal sex. No consistent associations were observed for other phthalate metabolites or BPA. Maternal exposure to DEHP during pregnancy was associated with decreased fetal growth, which could have repercussive effects.

hero.3466575

Fernandez, MA; André, LC; Cardeal, ZL. (2017). Hollow fiber liquid-phase microextraction-gas chromatography-mass spectrometry method to analyze bisphenol A and other plasticizer metabolites. J Chromatogr A 1481: 31-36. http://dx.doi.org/10.1016/j.chroma.2016.12.043.

Phthalates and bisphenol A are important environmental pollutants due to their toxicity for humans and animals, including actions in the endocrine system. Their metabolites in urine can be used as biomarkers to

assess human exposure. This paper describes the development of a new method to determine bisphenol A and eight phthalate metabolites in urine samples using hollow fiber liquid phase microextraction (HF-LPME) and gas chromatography-mass spectrometry (GC-MS). This method showed linearity, precision, limits of detection, and quantification suitable to analyze these compounds at low concentration levels in urine. Limits of detection ranged from 0.777 to 23.3µgL(-1), showing sensitivity for evaluating environmental exposure. Relative standard deviation (RSD) ranged from 11.7 to 19.7%. The developed method presented a good biomarker alternative for evaluating environmental exposure to bisphenol A and phthalates.

hero.3421301

Fiandanese, N; Borromeo, V; Berrini, A; Fischer, B; Schaedlich, K; Schmidt, JS; Secchi, C; P, P. (2016). Maternal exposure to a mixture of di(2-ethylhexyl) phthalate (DEHP) and polychlorinated biphenyls (PCBs) causes reproductive dysfunction in adult male mouse offspring. Reprod Toxicol 65: 123-132. http://dx.doi.org/10.1016/j.reprotox.2016.07.004.

We investigated the effects of maternal exposure to the plasticizer di(2-ethylhexyl) phthalate (DEHP) and the organic industrial compounds polychlorinated biphenyls (PCBs), singly and combined, on the reproductive function of male mouse offspring. Mice dams were exposed throughout pregnancy and lactation to 1 µg PCBs (101 + 118)/kg/day, 50 µg DEHP/kg/day, or the DEHP/PCB mixture in the diet. The mixture induced permanent alterations in adult F1 males reproductive health in a way, differently from the single compounds. Depending on the endpoint, we observed: (1) synergy in altering the gross and histological morphology of the testis; (2) antagonism on the expression levels of genes involved in pituitary-gonadal cross-talk; (3) non-interactions on sperm parameters and testosterone production. This study illustrates the complex action of a DEHP/PCB mixture, leading to a unique panel of effects on the male reproductive system, indicating the need for research on the reproductive hazards of combined endocrine disruptors.

hero.3469375 REVIEW

Foster, WG; Evans, JA; Little, J; Arbour, L; Moore, A; Sauve, R; Andrés León, J; Luo, W. (2016). Human exposure to environmental contaminants and congenital anomalies: a critical review. Crit Rev Toxicol1-26. http://dx.doi.org/10.1080/10408444.2016.1211090.

Congenital anomalies are an important cause of infant mortality and disability. Developmental exposure to environmental contaminants is thought to increase the risk for congenital anomalies. Herein, we describe a critical review of the literature conducted between February and March 2014 yielding 3057 references from which 97 unique relevant articles published from 2003 through 2014 were evaluated. Common congenital anomalies including hypospadias, cryptorchidism, anogenital distance (AGD), congenital heart defects and oral clefts were well represented in the literature whereas other outcomes such as neural tube defects, limb deficiency defects and gastroschisis were rarely described. While definitions used for congenital anomalies and methods of ascertainment were usually consistent across studies, inconsistencies were frequently found in grouping of different congenital heart defects. Despite strong links between some congenital anomalies and parental occupation, these studies are unable to provide clear insight into the specific chemicals responsible owing to lack of direct measures of exposure. In comparison, data are mixed for contaminant exposures at concentrations representative of results from contemporary biomonitoring studies. Of the environmental contaminants studied, the association between phthalate exposures and developmental abnormalities of the male reproductive tract received the greatest attention. Important limitations of the literature studied relate to adequacy of sample size, absence of or weaknesses in exposure assessment methodologies, failure to account for biological plausibility and grouping of congenital anomalies with divergent mechanisms. We conclude that the literature is inadequate at this time to support a conclusion that exposure to environmental contaminants are or are not associated with increased risks for congenital anomalies in the general population.

hero.3070939

Fournier, K; Tebby, C; Zeman, F; Glorennec, P; Zmirou-Navier, D; Bonvallot, N. (2016). Multiple exposures to indoor contaminants: Derivation of benchmark doses and relative potency factors based on male reprotoxic effects. Regul Toxicol Pharmacol 74: 23-30. http://dx.doi.org/10.1016/j.yrtph.2015.11.017.

Semi-Volatile Organic Compounds (SVOCs) are commonly present in dwellings and several are suspected of having effects on male reproductive function mediated by an endocrine disruption mode of action. To

improve knowledge of the health impact of these compounds, cumulative toxicity indicators are needed. This work derives Benchmark Doses (BMD) and Relative Potency Factors (RPF) for SVOCs acting on the male reproductive system through the same mode of action. We included SVOCs fulfilling the following conditions: detection frequency (>10%) in French dwellings, availability of data on the mechanism/mode of action for male reproductive toxicity, and availability of comparable dose-response relationships. Of 58 SVOCs selected, 18 induce a decrease in serum testosterone levels. Six have sufficient and comparable data to derive BMDs based on 10 or 50% of the response. The SVOCs inducing the largest decrease in serum testosterone concentration are: for 10%, bisphenol A (BMD10=7.72E-07mg/kg bw/d; RPF10=7,033,679); for 50%, benzo[a]pyrene (BMD50=0.030mg/kg bw/d; RPF50=1630), and the one inducing the smallest one is benzyl butyl phthalate (RPF10 and RPF50=0.095). This approach encompasses contaminants from diverse chemical families acting through similar modes of action, and makes possible a cumulative risk assessment in indoor environments. The main limitation remains the lack of comparable toxicological data.

hero.3445439

Franken, C; Koppen, G; Lambrechts, N; Govarts, E; Bruckers, L; Den Hond, E; Loots, I; Nelen, V; Sioen, I; Nawrot, TS; Baeyens, W; Van Larebeke, N; Boonen, F; Ooms, D; Wevers, M; Jacobs, G; Covaci, A; Schettgen, T; Schoeters, G. (2016). Environmental exposure to human carcinogens in teenagers and the association with DNA damage. Environ Res 152: 165-174. http://dx.doi.org/10.1016/j.envres.2016.10.012.
BACKGROUND: We investigated whether human environmental exposure to chemicals that are labeled as (potential) carcinogens leads to increased (oxidative) damage to DNA in adolescents.

MATERIAL AND METHODS: Six hundred 14-15-year-old youngsters were recruited all over Flanders (Belgium) and in two areas with important industrial activities. DNA damage was assessed by alkaline and formamidopyrimidine DNA glycosylase (Fpg) modified comet assays in peripheral blood cells and analysis of urinary 8-hydroxydeoxyguanosine (8-OHdG) levels. Personal exposure to potentially carcinogenic compounds was measured in urine, namely: chromium, cadmium, nickel, 1-hydroxypyrene as a proxy for exposure to other carcinogenic polycyclic aromatic hydrocarbons (PAHs), t,t-muconic acid as a metabolite of benzene, 2,5-dichlorophenol (2,5-DCP), organophosphate pesticide metabolites, and di(2-ethylhexyl) phthalate (DEHP) metabolites. In blood, arsenic, polychlorinated biphenyl (PCB) congeners 118 and 156, hexachlorobenzene (HCB), dichlorodiphenyltrichloroethane (DDT) and perfluorooctanoic acid (PFOA) were analyzed. Levels of methylmercury (MeHg) were measured in hair. Multiple linear regression models were used to establish exposure-response relationships.

RESULTS: Biomarkers of exposure to PAHs and urinary chromium were associated with higher levels of both 8-OHdG in urine and DNA damage detected by the alkaline comet assay. Concentrations of 8-OHdG in urine increased in relation with increasing concentrations of urinary t,t-muconic acid, cadmium, nickel, 2,5-DCP, and DEHP metabolites. Increased concentrations of PFOA in blood were associated with higher levels of DNA damage measured by the alkaline comet assay, whereas DDT was associated in the same direction with the Fpg-modified comet assay. Inverse associations were observed between blood arsenic, hair MeHg, PCB 156 and HCB, and urinary 8-OHdG. The latter exposure biomarkers were also associated with higher fish intake. Urinary nickel and t,t-muconic acid were inversely associated with the alkaline comet assay.

CONCLUSION: This cross-sectional study found associations between current environmental exposure to (potential) human carcinogens in 14-15-year-old Flemish adolescents and short-term (oxidative) damage to DNA. Prospective follow-up will be required to investigate whether long-term effects may occur due to complex environmental exposures.

hero.3479557

Fu, H; Tisdale, S; Schaffer, M; IEEE. (2016). Framework for Implementing Material Alternatives Assessment. 99-104.
For the electronics and semiconductor industries, as well as for suppliers in the chemical industry where new, complex material development has a key role in advancing the next technology innovations, a proactive approach to addressing Environmental, Health and Safety (EHS) issues is a critical necessity, given lengthy development times. There are many tools currently available to industry that can assist in the evaluation of alternative materials and lead to more informed and better decisions with respect to the materials used to make products. At this time, there is no uniform methodology within governments, NGOs, academia or industry for examining new or alternative materials for environmental, safety or human health impacts. As a result, chemical restrictions are inconsistent and can negatively impact the product roadmaps of electronics

and semiconductor manufacturers, which often take years for development. Alternative materials assessment is a key factor in developing policies that are more holistic in nature and allow for better risk mitigation to be included in product choices at the source. A consistent method and framework of evaluation of existing methods will provide the opportunity for material selection that is safer, less hazardous and more sustainable than the more typical "banning" solution often specified in policy like RoHS today.

The iNEMI (International Electronics Manufacturing Initiative) project on Alternative Materials Assessment examined key existing materials assessment strategies (frameworks, methodologies and tools), for the application and effectiveness in evaluating their environmental/toxicological properties for use. The team has taken a phased approach and conducted a focused benchmarking exercise, using several representative, industry-relevant chemical substances (Phthalates, NMP and TBBP-A), as a means of comparing a carefully selected list of assessment tools, which have potential for broad use in the near future. A gap analysis summary and comparison of key descriptors and key tool use criteria was evaluated for these representative substances, creating an important reference document that can serve to standardize and streamline the approach to alternative assessment. The intent of this study was to facilitate a more proactive, better informed decision making process, for more effective risk mitigation. A summary of the results of our evaluation and potential next steps were provided in the end-of project report, now published on the iNEMI website.

hero.3469334

Fulcher, YG; Fotso, M; Chang, CH; Rindt, H; Reinero, CR; Van Doren, SR. (2016). Noninvasive Recognition and Biomarkers of Early Allergic Asthma in Cats Using Multivariate Statistical Analysis of NMR Spectra of Exhaled Breath Condensate. PLoS ONE 11: e0164394. http://dx.doi.org/10.1371/journal.pone.0164394.
Asthma is prevalent in children and cats, and needs means of noninvasive diagnosis. We sought to distinguish noninvasively the differences in 53 cats before and soon after induction of allergic asthma, using NMR spectra of exhaled breath condensate (EBC). Statistical pattern recognition was improved considerably by preprocessing the spectra with probabilistic quotient normalization and glog transformation. Classification of the 106 preprocessed spectra by principal component analysis and partial least squares with discriminant analysis (PLS-DA) appears to be impaired by variances unrelated to eosinophilic asthma. By filtering out confounding variances, orthogonal signal correction (OSC) PLS-DA greatly improved the separation of the healthy and early asthmatic states, attaining 94% specificity and 94% sensitivity in predictions. OSC enhancement of multi-level PLS-DA boosted the specificity of the prediction to 100%. OSC-PLS-DA of the normalized spectra suggest the most promising biomarkers of allergic asthma in cats to include increased acetone, metabolite(s) with overlapped NMR peaks near 5.8 ppm, and a hydroxyphenyl-containing metabolite, as well as decreased phthalate. Acetone is elevated in the EBC of 74% of the cats with early asthma. The noninvasive detection of early experimental asthma, biomarkers in EBC, and metabolic perturbation invite further investigation of the diagnostic potential in humans.

hero.3479508

Gabb, HA; Blake, C. (2016). An Informatics Approach to Evaluating Combined Chemical Exposures from Consumer Products: A Case Study of Asthma-Associated Chemicals and Potential Endocrine Disruptors. Environ Health Perspect 124: 1155-1165. http://dx.doi.org/10.1289/ehp.1510529.
BACKGROUND: Simultaneous or sequential exposure to multiple environmental stressors can affect chemical toxicity. Cumulative risk assessments consider multiple stressors but it is impractical to test every chemical combination to which people are exposed. New methods are needed to prioritize chemical combinations based on their prevalence and possible health impacts.

OBJECTIVES: We introduce an informatics approach that uses publicly available data to identify chemicals that co-occur in consumer products, which account for a significant proportion of overall chemical load.

METHODS: Fifty-five asthma-associated and endocrine disrupting chemicals (target chemicals) were selected. A database of 38,975 distinct consumer products and 32,231 distinct ingredient names was created from online sources, and PubChem and the Unified Medical Language System were used to resolve synonymous ingredient names. Synonymous ingredient names are different names for the same chemical (e.g., vitamin E and tocopherol).

RESULTS: Nearly one-third of the products (11,688 products, 30%) contained 1 target chemical and 5,229 products (13%) contained > 1. Of the 55 target chemicals, 31 (56%) appear in 1

product and 19 (35%) appear under more than one name. The most frequent three-way chemical combination (2-phenoxyethanol, methyl paraben, and ethyl paraben) appears in 1,059 products. Further work is needed to assess combined chemical exposures related to the use of multiple products.

 CONCLUSIONS: The informatics approach increased the number of products considered in a traditional analysis by two orders of magnitude, but missing/incomplete product labels can limit the effectiveness of this approach. Such an approach must resolve synonymy to ensure that chemicals of interest are not missed. Commonly occurring chemical combinations can be used to prioritize cumulative toxicology risk assessments.

CITATION: Gabb HA, Blake C. 2016. An informatics approach to evaluating combined chemical exposures from consumer products: a case study of asthma-associated chemicals and potential endocrine disruptors. Environ Health Perspect 124:1155-1165; http://dx.doi.org/10.1289/ehp.1510529.

hero.3350668

Gaberšček, S; Zaletel, K. (2016). Epidemiological trends of iodine-related thyroid disorders: an example from Slovenia. Arh Hig Rada Toksikol 67: 93-98. http://dx.doi.org/10.1515/aiht-2016-67-2725.

The epidemiology of thyroid disorders is significantly associated with iodine supply. In 1999, Slovenia increased iodine content in kitchen salt from 10 mg to 25 mg of potassium iodide per kg of salt. According to the WHO criteria, Slovenia shifted from a mildly iodine-deficient country to a country with adequate iodine intake. Ten years after the increase in iodine intake, the incidence of diffuse goitre and thyroid autonomy decreased. Now patients with diffuse goitre and thyroid autonomy reach older age than the patients before the increase in iodine intake. In addition, patients with thyroid autonomy are less frequently hyperthyroid than ten years ago and iodine-induced hyperthyroidism is less severe. The incidence of highly malignant thyroid carcinoma has also dropped. However, the incidence of Hashimoto's thyroiditis increased, most probably in genetically predisposed individuals. Over the last ten years, many animal and in vitro studies evaluated the effects of endocrine disrupting chemicals (EDC) on various aspects of the thyroid function. They mostly studied the effects of polychlorinated biphenyls (PCBs) and dioxins, brominated flame retardants, phthalates, bisphenol A, perfluorinated chemicals, and perchlorate. However, human studies on the effects of EDCs on the thyroid function are very scarce, especially the long-term ones. What they do suggest is that PCBs and dioxins interfere with the transport of thyroid hormones and adversely affect the thyroid function. Many authors agree that iodine deficiency predisposes the thyroid gland to harmful effects of EDCs. Therefore the effects of EDCs in iodine-deficient areas could be more severe than in areas with adequate iodine intake.

hero.3350189

Gani, KM; Kazmi, AA. (2016). Comparative assessment of phthalate removal and risk in biological wastewater treatment systems of developing countries and small communities. Sci Total Environ 569-570: 661-671. http://dx.doi.org/10.1016/j.scitotenv.2016.06.182.

Phthalates are widely used in plastic and personnel care products. Being non-steroid endocrine disrupting compounds, their exposure have toxic effects on aquatic life and human health. The aim of this study was a comparative assessment of their fate and risk in full scale wastewater treatment along with influence of seasonal variations. Four priority phthalates, Diethylphthalate (DEP), Dibutylphthalate (DBP), Benzylbutyl phthalate (BBP) and Diethylhexyl phthalate (DEHP) were chosen for this study and wastewater treatment plants investigated were designed as nutrient removal based sequencing batch reactor (SBR), conventional activated sludge process (ASP) and up flow anaerobic sludge blanket (UASB) with polishing pond. Results showed that the main removal mechanism of phthalates was biotransformation with removal contribution of 74% in SBR, 65% in conventional ASP and 37% in UASB. Overall removal of phthalates was maximum in the treatment combination of UASB and pond (83%) followed by SBR (80%) and conventional ASP (74%). Seasonal influences on occurrence, removal and risk of these phthalates were also studied. The concentration of DEP, DBP and DEHP in untreated wastewater increased by 2, 7 and 2μg/L, respectively in summer. However in sludge, only large molecular weight phthalates BBP and DEHP increased in winter by 3mg/kg and 12mg/kg, respectively. Seasonal variations in removal of phthalates were discrepant in each process with better removal during summer. Risk assessment of phthalates to aquatic life showed that there is no potential risk of DEP, DBP and BBP from effluents of treatment plants however risk quotient of DEHP was in the range of 27-73 in both seasons which indicate probable risk to aquatic organisms. Phthalate risk

to human beings estimated by daily intake of phthalates was in the range of 0.30.1 to 200.7ng/kg/d and far below their respective reference dosages, demonstrating the potential of these treatment plants to reduce the risk of phthalates.

hero.3466571

Gao, H; Xu, YY; Huang, K; Ge, X; Zhang, YW; Yao, HY; Xu, YQ; Yan, SQ; Jin, ZX; Sheng, J; Zhu, P; Hao, JH; Tao, FB. (2016). Cumulative risk assessment of phthalates associated with birth outcomes in pregnant Chinese women: A prospective cohort study. Environ Pollut. http://dx.doi.org/10.1016/j.envpol.2016.11.026.

A prospective cohort study of a Chinese population of mother-neonate pairs (n=3103) was conducted to investigate the relationship between the cumulative hazard index (HI) of combined diethyl phthalate (DEP), dibutyl phthalate (DBP), dibenzyl phthalate (BBzP) and di(2-ethylhexyl) phthalate (DEHP) exposure and birth outcomes. The estimated HI for phthalates was based on phthalate metabolite concentrations in urine collected between 5th and 14th gestational weeks. The median HI values according to the European Food Safety Authority tolerable daily intake (HITDI) and U.S. Environmental Protection Agency reference dose (HIRfD) were 0.358 and 0.187, respectively. A total of 16.3% and 1.9% of the women exhibited HITDI and HIRfD exceeding the value of one, respectively. In unadjusted models, the categories (low<P25, median P25-P50, high>P75) of HITDI were associated with decreased birth weight (β=-26.34g, p=0.021) and head circumference (β=-0.09cm, p=0.029), whereas those for HIRfD were negatively associated with birth weight (β=-31.74g, p=0.005), birth length (β=-0.11cm, p=0.032), head circumference (β=-0.13cm, p=0.003) and chest circumference (β=-0.10cm, p=0.021) in all neonates. Adjustment for potential confounders revealed that HIRfD was inversely associated with head circumference (β=-0.10cm, p=0.020). Stratification by gender indicated that HIRfD was associated with decreased birth length (β=-0.17cm, p=0.041) in infant boys and HITDI was associated with decreased birth weight (β=-33.12g, p=0.036) and head circumference (β=-0.13cm, p=0.027) in girls. This is the first study on the cumulative risk assessment of phthalate exposures in pregnant Chinese women. We found that the HI values of multiple phthalate co-exposure were sex-specifically related to birth outcomes.

hero.3469450

Gao, HT; Xu, R; Cao, WX; Zhou, X; Yan, YH; Lu, L; Xu, Q; Shen, Y. (2016). Food Emulsifier Glycerin Monostearate Increases Internal Exposure Levels of Six Priority Controlled Phthalate Esters and Exacerbates Their Male Reproductive Toxicities in Rats. PLoS ONE 11: e0161253. http://dx.doi.org/10.1371/journal.pone.0161253.

Human beings are inevitably exposed to ubiquitous phthalate esters (PAEs). Processed, packaged foods are popular nowadays, in which emulsifiers are frequently added as food additives. It is unclear how emulsifiers affect the bioavailability of ingested PAEs contaminants and their toxicities. The purposes of our study were to explore whether food emulsifier Glycerin Monostearate (GMS) could increase the internal exposure levels of six priority controlled PAEs and affect their reproductive toxicities when male rats are exposed to PAEs mixture (MIXPs). The male rats were exposed to MIXPs by gavage for thirty days in combination with or without given GMS. Phthalate monoesters (MPAEs), primary metabolites of PAEs, in rat urine were used as biomarkers to predict the internal exposure levels of the six PAEs, and their concentrations were determined using UPLC-MS. The reproductive toxicity was evaluated using serum testosterone levels test and histopathology of testes. Results showed that compared to PAEs exposure alone, the internal exposure levels of PAEs increased by 30%-49% in the presence of GMS. PAEs exposure led to the reduction of testosterone level by 23.4%-42.1% in the presence and absence of GMS, respectively, compared to the baseline. Testosterone levels in MIXPs+GMS and DEHP+GMS group were decreased by 9.1% and 13.6%, respectively, compared with MIXPs and DEHP group. Histopathology showed that injuries of testis (deciduous spermatids) were observed, and GMS exacerbated the injuries. The results indicated food emulsifiers chronically taken up might increase safety risks of food PAEs contaminants.

hero.3350313

Garg, A; Rai, G; Lodhi, S; Jain, AP; Yadav, AK. (2016). Hyaluronic acid embedded cellulose acetate phthlate core/shell nanoparticulate carrier of 5-fluorouracil. Int J Biol Macromol 87: 449-459. http://dx.doi.org/10.1016/j.ijbiomac.2015.11.094.

Aim of this research was to prepare hyaluronic acid-modified-cellulose acetate phthalate (HAC) core shell nanoparticles (NPs) of 5-fluorouracil (5-FU). HAC copolymer was synthesized and confirmed by fourier

transform infrared (FTIR) and nuclear magnetic resonance (NMR) spectroscopy. HAC NPs with 5-FU were prepared using HAC copolymer and compared with 5-FU loaded cellulose acetate phthalate (CAP) NPs. NPs were characterized by atomic force microscopy (AFM), particle size, zeta potential, polydispersity index, entrapment efficiency, in-vitro release, differential scanning calorimetry (DSC) and X-ray diffraction (XRD). HAC NPs were found slower release (97.30% in 48h) than (99.25% in 8h) CAP NPs. In cytotoxicity studies, showed great cytotoxic potential of 5-FU loaded HAC NPs in A549, MDA-MD-435 and SK-OV-3 cancer cellline. HAC NPs showing least hemolytic than CAP NPs and 5-FU. Area under curve (AUC), maximum plasma concentration (Cmax), mean residence time (MRT) and time to reach maximum plasma concentration Tmax), were observed 4398.17.90µgh/mL, 145.452.25µg/L, 45.740.25h, 720.50h, respectively of HAC NPs and 119.921.78µgh/mL, 46.383.42µg/L, 1.20.25h, 0.50.02h were observed in plain 5-FU solution. In conclusion, HAC NPs is effective deliver carrier of 5-FU for lung cancer.

hero.3468133

Ge, WP; Yang, XJ; Wu, XY; Wang, Z; Geng, W; Guo, CF. (2016). Phthalate residue in goat milk-based infant formulas manufactured in China. J Dairy Sci 99: 7776-7781. http://dx.doi.org/10.3168/jds.2016-11061.

Phthalates adversely affect the male reproductive system in humans. Through gas chromatography-mass spectrometry analysis, we investigated the residual profile and levels of 15 phthalates in 90 goat milk-based infant formulas from 15 commercial brands of 10 dairy enterprises located in Shaanxi Province, China. In general, dibutyl phthalate was the most detected phthalate, followed by bis(2-ethylhexyl) phthalate, diisobutyl phthalate, and dimethyl phthalate; their geometric mean concentrations in the formulas were 38.1, 24.2, 16.6, and 8.7µg/kg, respectively. Other phthalates were not detected in the investigated samples. No significant differences were found in the phthalate levels among different stages of infant formulas, even though the samples were packaged in different types of containers. These findings demonstrate that goat milk-based infant formulas may represent the main source of exposure to phthalates in infants.

hero.3479529

Giesbrecht, GF; Liu, J; Ejaredar, M; Dewey, D; Letourneau, N; Campbell, T; Martin, JW; Team, AS. (2016). Urinary bisphenol A is associated with dysregulation of HPA-axis function in pregnant women: Findings from the APrON cohort study. Environ Res 151: 689-697. http://dx.doi.org/10.1016/j.envres.2016.09.007.

BACKGROUND: Bisphenol A (BPA) is associated with dysregulation of hypothalamic-pituitary-adrenal (HPA) axis activity in rodents, but evidence in humans is lacking.

OBJECTIVE: To determine whether BPA exposure during pregnancy is associated with dysregulation of the HPA-axis, we examined the association between urinary BPA concentrations and diurnal salivary cortisol in pregnant women. Secondary analyses investigated whether the association between BPA and cortisol was dependent on fetal sex.

METHODS: Diurnal salivary cortisol and urinary BPA were collected during pregnancy from 174 women in a longitudinal cohort study, the Alberta Pregnancy Outcomes and Nutrition (APrON) study. Associations between BPA and daytime cortisol and the cortisol awakening response (CAR) were estimated using mixed models after adjusting for covariates.

RESULTS: Higher concentrations of total BPA uncorrected for urinary creatinine were associated with dysregulation of the daytime cortisol pattern, including reduced cortisol at waking, β=-.055, 95% CI (-.100, -.010) and a flatter daytime pattern, β=.014, 95% CI (.006, .022) and β=-.0007 95% CI (-.001, -.0002) for the linear and quadratic slopes, respectively. Effect sizes in creatinine corrected BPA models were slightly smaller. None of the interactions between fetal sex and BPA were significant (all 95% CI's include zero).

CONCLUSIONS: These findings provide the first human evidence suggesting that BPA exposure is associated with dysregulation of HPA-axis function during pregnancy.

hero.3350192 REVIEW

Ginsberg, G; Ginsberg, J; Foos, B. (2016). Approaches to Children's Exposure Assessment: Case Study with Diethylhexylphthalate (DEHP) [Review]. Int J Environ Res Public Health 13. http://dx.doi.org/10.3390/ijerph13070670.

Children's exposure assessment is a key input into epidemiology studies, risk assessment and source apportionment. The goals of this article are to describe a methodology for children's exposure assessment that can be used for these purposes and to apply the methodology to source apportionment for the case

study chemical, diethylhexylphthalate (DEHP). A key feature is the comparison of total (aggregate) exposure calculated via a pathways approach to that derived from a biomonitoring approach. The 4-step methodology and its results for DEHP are: (1) Prioritization of life stages and exposure pathways, with pregnancy, breast-fed infants, and toddlers the focus of the case study and pathways selected that are relevant to these groups; (2) Estimation of pathway-specific exposures by life stage wherein diet was found to be the largest contributor for pregnant women, breast milk and mouthing behavior for the nursing infant and diet, house dust, and mouthing for toddlers; (3) Comparison of aggregate exposure by pathways vs biomonitoring-based approaches wherein good concordance was found for toddlers and pregnant women providing confidence in the exposure assessment; (4) Source apportionment in which DEHP presence in foods, children's products, consumer products and the built environment are discussed with respect to early life mouthing, house dust and dietary exposure. A potential fifth step of the method involves the calculation of exposure doses for risk assessment which is described but outside the scope for the current case study. In summary, the methodology has been used to synthesize the available information to identify key sources of early life exposure to DEHP.

hero.3455194

Giovanoulis, G; Alves, A; Papadopoulou, E; Cousins, AP; Schütze, A; Koch, HM; Haug, LS; Covaci, A; Magnér, J; Voorspoels, S. (2016). Evaluation of exposure to phthalate esters and DINCH in urine and nails from a Norwegian study population. Environ Res 151: 80-90. http://dx.doi.org/10.1016/j.envres.2016.07.025.

Phthalate esters (PEs) and 1,2-cyclohexane dicarboxylic acid diisononyl ester (DINCH) used as additives in numerous consumer products are continuously released into the environment, leading to subsequent human exposure which might cause adverse health effects. The human biomonitoring approach allows the detection of PEs and DINCH in specific populations, by taking into account all possible routes of exposure (e.g. inhalation, transdermal and oral) and all relevant sources (e.g. air, dust, personal care products, diet). We have investigated the presence of nine PE and two DINCH metabolites and their exposure determinants in 61 adult residents of the Oslo area (Norway). Three urine spots and fingernails were collected from each participant according to established sampling protocols. Metabolite analysis was performed by LC-MS/MS. Metabolite levels in urine were used to back-calculate the total exposure to their corresponding parent compound. The primary monoesters, such as monomethyl phthalate (MMP, geometric mean 89.7ng/g), monoethyl phthalate (MEP, 104.8ng/g) and mono-n-butyl phthalate (MnBP, 89.3ng/g) were observed in higher levels in nails, whereas the secondary bis(2-ethylhexyl) phthalate (DEHP) and DINCH oxidative metabolites were more abundant in urine (detection frequency 84-100%). The estimated daily intakes of PEs and DINCH for this Norwegian population did not exceed the established tolerable daily intake and reference doses, and the cumulative risk assessment for combined exposure to plasticizers with similar toxic endpoints indicated no health concerns for the selected population. We found a moderate positive correlation between MEP levels in 3 urine spots and nails (range: 0.56-0.68). Higher frequency of personal care products use was associated with greater MEP concentrations in both urine and nail samples. Increased age, smoking, wearing plastic gloves during house cleaning, consuming food with plastic packaging and eating with hands were associated with higher levels in urine and nails for some of the metabolites. In contrast, frequent hair and hand washing was associated with lower urinary levels of monoisobutyl phthalate (MiBP) and mono(2-ethyl-5-hydroxyhexyl) phthalate (5-OH-MEHP), respectively.

hero.3469349 REVIEW

Giulivo, M; Lopez de Alda, M; Capri, E; Barceló, D. (2016). Human exposure to endocrine disrupting compounds: Their role in reproductive systems, metabolic syndrome and breast cancer. A review [Review]. Environ Res 151: 251-264. http://dx.doi.org/10.1016/j.envres.2016.07.011.

Endocrine disrupting chemicals (EDCs) are released into the environment from different sources. They are mainly used in packaging industries, pesticides and food constituents. Clinical evidence, experimental models, and epidemiological studies suggest that EDCs have major risks for humans by targeting different organs and systems in the body (e.g. reproductive system, breast tissue, adipose tissue, pancreas, etc.). Due to the ubiquity of human exposure to these compounds the aim of this review is to describe the most recent data on the effects induced by phthalates, bisphenol A and parabens in a critical window of exposure: in utero, during pregnancy, infants, and children. The interactions and mechanisms of toxicity of EDCs in relation to human general health problems, especially those broadening the term of endocrine disruption to

'metabolic disruption', should be deeply investigated. These include endocrine disturbances, with particular reference to reproductive problems and breast, testicular and ovarian cancers, and metabolic diseases such as obesity or diabetes.

hero.3350817

Goho, SA. (2016). The Legal Implications of Report-Back in Household Exposure Studies [Review]. Environ Health Perspect 124: 1662-1670. http://dx.doi.org/10.1289/EHP187.

BACKGROUND: Scientists conducting research into household air or dust pollution must decide whether, when, and how to disclose to study participants their individual results. A variety of considerations factor into this decision, but one factor that has not received attention until now is the possibility that study participants' receipt of their results might create legal duties under environmental, property, landlord-tenant, or other laws.

OBJECTIVES & METHODS: This review examines relevant laws and regulations and explores the scope of participants' legal duties and the resulting legal and ethical consequences for researchers. Participants could be required in some situations to disclose the presence of certain chemicals when selling or renting their homes or to frequent visitors. The review discusses hypothetical case studies involving the report-back of results regarding lead, PCBs, parabens, and phthalates.

DISCUSSION: Study participants' potential legal duties have both ethical and legal implications for researchers. Issues include whether the legal consequences for participants should affect the decision whether to report-back individual results, how researchers should disclose the legal risks to participants during the informed consent process, and whether researchers would be liable to study participants for legal or economic harm arising from reporting study results to them. The review provides recommendations for language that researchers could use in the informed consent process to disclose the legal risks.

CONCLUSIONS: Researchers should still report back results to participants who want them, but should disclose these risks as part of the informed consent process.

hero.3159455

Gołębiowski, M; Stepnowski, P; Hemmingway, T; Leszczyńska, D. (2016). Organic compound composition in soil and sediments collected in Jackson, Mississippi. J Environ Sci Health A Tox Hazard Subst Environ Eng 51: 553-560. http://dx.doi.org/10.1080/10934529.2016.1141621.

The aim of our study was to identify organic pollutants found in soil and sediment samples collected within the Jackson, MS metropolitan area. The chemical characterization of the organic compound fractions in soil and sediment samples was carried out by separating the organic fraction using column chromatography (CC) and quantitatively analyzing the polycyclic aromatic hydrocarbons (PAHs), n-alkanes and other organic compounds using gas chromatography-electron impact mass spectrometry (GC-MS). Fifty-six compounds were identified and quantified in the soil samples and 33 compounds were identified and quantified in the sediment samples. The PAHs, n-alkanes and other organic compound profiles in the soil and sediment samples were compared. The percentage contents of the organic compounds in the soil samples were very diverse (from traces to 12.44 1.47%). The compounds present in the highest concentrations were n-alkanes: n-C31 (12.44 1.47%), n-C29 (11.64 1.21%), and n-C33 (8.95 1.08%). The components occurring in smaller quantities (from 1% to 5%) were 2 PAHs (fluoranthene 1.28 0.25%, pyrene 1.16 0.20%), 10 n-alkanes from n-C21 (1.25 0.29%) to n-C32 (2.67 0.52%) and 11 other compounds (e.g., 2-pentanol, 4-methyl (3.33 0.44%), benzyl butyl phthalate (4.25 0.59%), benzenedicarboxylic acid (1.14 0.08%), ethane, 1,1-diethoxy (3.15 0.41) and hexadecanoic acid (2.52 0.34). The soil samples also contained 30 compounds present in concentrations <1% (e.g., anthracene (0.13 0.04%), n-C20 (0.84 0.21%) and acetic acid (0.12 0.04%). The compounds present in the highest concentrations in the sediment samples were PAHs: pyrene (7.73 1.15%) and fluoranthene (6.23 1.07%) and n-alkanes: n-C31 (6.74 1.21%), n-C29 (6.65 0.98%) and n-C27 (6.13 1.09%). The remaining organic compounds were present in smaller quantities (< 5%).

hero.3469549

Gonzalez, NL; O'Brien, KM; D'Aloisio, AA; Sandler, DP; Weinberg, CR. (2016). Douching, Talc Use, and Risk of Ovarian Cancer. Epidemiology 27: 797-802. http://dx.doi.org/10.1097/EDE.0000000000000528.

BACKGROUND: Douching was recently reported to be associated with elevated levels of urinary metabolites of endocrine disrupting phthalates, but there is no literature on douching in relation to

ovarian cancer. Numerous case-control studies of genital talc use have reported an increased risk of ovarian cancer, but prospective cohort studies have not uniformly confirmed this association. Behavioral correlation between talc use and douching could produce confounding.

METHODS: The Sister Study (2003-2009) enrolled and followed 50,884 women in the US and Puerto Rico who had a sister diagnosed with breast cancer. At baseline, participants were asked about douching and talc use during the previous 12 months. During follow-up (median of 6.6 years), 154 participants reported a diagnosis of ovarian cancer. We computed adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for ovarian cancer risk using the Cox proportional hazards model.

RESULTS: There was little association between baseline perineal talc use and subsequent ovarian cancer (HR: 0.73, CI: 0.44, 1.2). Douching was more common among talc users (odds ratio: 2.1, CI: 2.0, 2.3), and douching at baseline was associated with increased subsequent risk of ovarian cancer (HR: 1.8, CI: 1.2, 2.8).

CONCLUSIONS: Douching but not talc use was associated with increased risk of ovarian cancer in the Sister Study.

hero.3479552

Gonzalez-Bulnes, A; Astiz, S; Ovilo, C; Garcia-Contreras, C; Vazquez-Gomez, M. (2016). Nature and Nurture in the Early-Life Origins of Metabolic Syndrome. Curr Pharm Biotechnol 17: 573-586. http://dx.doi.org/10.2174/1389201017666160301103835.

The combination of genetic background together with food excess and lack of exercise has become the cornerstone of metabolic disorders associated to lifestyle. The scenario is furthermore reinforced by their interaction with other environmental factors (stress, sleeping patterns, education, culture, rural versus urban locations, and xenobiotics, among others) inducing epigenetic changes in the exposed individuals. The immediate consequence is the development of further alterations like obesity and metabolic syndrome, and other adverse health conditions (type-2 diabetes, cardiovascular diseases, cancer, reproductive, immune and neurological disorders). Thus, having in mind the impact of the metabolic syndrome on the worldwide public health, the present review affords the relative roles and the interrelationships of nature (genetic predisposition to metabolic syndrome) and nurture (lifestyle and environmental effects causing epigenetic changes), on the establishment of the metabolic disorders in women; disorders that may evolve to metabolic syndrome prior or during pregnancy and may be transmitted to their descendants.

hero.3178997 REVIEW

Gore, AC; Chappell, VA; Fenton, SE; Flaws, JA; Nadal, A; Prins, GS; Toppari, J; Zoeller, RT. (2015). EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocr Rev 36: E1-E150. http://dx.doi.org/10.1210/er.2015-1010.

The Endocrine Society's first Scientific Statement in 2009 provided a wake-up call to the scientific community about how environmental endocrine-disrupting chemicals (EDCs) affect health and disease. Five years later, a substantially larger body of literature has solidified our understanding of plausible mechanisms underlying EDC actions and how exposures in animals and humans-especially during development-may lay the foundations for disease later in life. At this point in history, we have much stronger knowledge about how EDCs alter gene-environment interactions via physiological, cellular, molecular, and epigenetic changes, thereby producing effects in exposed individuals as well as their descendants. Causal links between exposure and manifestation of disease are substantiated by experimental animal models and are consistent with correlative epidemiological data in humans. There are several caveats because differences in how experimental animal work is conducted can lead to difficulties in drawing broad conclusions, and we must continue to be cautious about inferring causality in humans. In this second Scientific Statement, we reviewed the literature on a subset of topics for which the translational evidence is strongest: 1) obesity and diabetes; 2) female reproduction; 3) male reproduction; 4) hormone-sensitive cancers in females; 5) prostate; 6) thyroid; and 7) neurodevelopment and neuroendocrine systems. Our inclusion criteria for studies were those conducted predominantly in the past 5 years deemed to be of high quality based on appropriate negative and positive control groups or populations, adequate sample size and experimental design, and mammalian animal studies with exposure levels in a range that was relevant to humans. We also focused on studies using the developmental origins of health and disease model. No report was excluded based on a positive or negative effect of the EDC exposure. The bulk of the results across the board strengthen the evidence for endocrine health-related actions of EDCs. Based on this much more complete understanding of the

endocrine principles by which EDCs act, including nonmonotonic dose-responses, low-dose effects, and developmental vulnerability, these findings can be much better translated to human health. Armed with this information, researchers, physicians, and other healthcare providers can guide regulators and policymakers as they make responsible decisions.

hero.3351214 REVIEW

Gore, AC; Chappell, VA; Fenton, SE; Flaws, JA; Nadal, A; Prins, GS; Toppari, J; Zoeller, RT. (2015). Executive Summary to EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocr Rev 36: 593-602. http://dx.doi.org/10.1210/er.2015-1093.

This Executive Summary to the Endocrine Society's second Scientific Statement on environmental endocrine-disrupting chemicals (EDCs) provides a synthesis of the key points of the complete statement. The full Scientific Statement represents a comprehensive review of the literature on seven topics for which there is strong mechanistic, experimental, animal, and epidemiological evidence for endocrine disruption, namely: obesity and diabetes, female reproduction, male reproduction, hormone-sensitive cancers in females, prostate cancer, thyroid, and neurodevelopment and neuroendocrine systems. EDCs such as bisphenol A, phthalates, pesticides, persistent organic pollutants such as polychlorinated biphenyls, polybrominated diethyl ethers, and dioxins were emphasized because these chemicals had the greatest depth and breadth of available information. The Statement also included thorough coverage of studies of developmental exposures to EDCs, especially in the fetus and infant, because these are critical life stages during which perturbations of hormones can increase the probability of a disease or dysfunction later in life. A conclusion of the Statement is that publications over the past 5 years have led to a much fuller understanding of the endocrine principles by which EDCs act, including nonmonotonic dose-responses, low-dose effects, and developmental vulnerability. These findings will prove useful to researchers, physicians, and other healthcare providers in translating the science of endocrine disruption to improved public health.

hero.3071006

Gray, LE; Furr, J; Tatum-Gibbs, KR; Lambright, C; Sampson, H; Hannas, BR; Wilson, VS; Hotchkiss, A; Foster, PM. (2016). Establishing the "Biological Relevance" of Dipentyl Phthalate Reductions in Fetal Rat Testosterone Production and Plasma and Testis Testosterone Levels. Toxicol Sci 149: 178-191. http://dx.doi.org/10.1093/toxsci/kfv224.

Phthalate esters (PEs) constitute a large class of compounds that are used for many consumer product applications. Many of the C2-C7 di-ortho PEs reduce fetal testicular hormone and gene expression levels in rats resulting in adverse effects seen later in life but it appears that relatively large reductions in fetal testosterone (T) levels and testis gene expression may be required to adversely affect reproductive development (Hannas, B. R., Lambright, C. S., Furr, J., Evans, N., Foster, P. M., Gray, E. L., and Wilson, V. S. (2012). Genomic biomarkers of phthalate-induced male reproductive developmental toxicity: a targeted RT-PCR array approach for defining relative potency. Toxicol. Sci. 125, 544-557). The objectives of this study were (1) to model the relationships between changes in fetal male rat plasma testosterone (PT), T levels in the testis (TT), T production (PROD), and testis gene expression with the reproductive malformation rates, and (2) to quantify the "biologically relevant reductions" (BRRs) in fetal T necessary to induce adverse effects in the offspring. In the fetal experiment, Harlan Sprague-Dawley rats were dosed with dipentyl phthalate (DPeP) at 0, 11, 33, 100, and 300 mg/kg/day from gestational days (GD) 14-18 and fetal testicular T, PT levels, and T Prod and gene expression were assessed on GD 18. In the postnatal experiment, rats were dosed with DPeP from GD 8-18 and reproductive development was monitored through adulthood. The dose-response curves for TT levels (ED50 = 53 mg/kg) and T PROD (ED50 = 45 mg/kg) were similar, whereas PT was reduced at ED50 = 19 mg/kg. When the reductions in TPROD and Insl3 mRNA were compared with the postnatal effects of in utero DPeP, dose-related reproductive alterations were noted when T PROD and Insl3 mRNA were reduced by >45% and 42%, respectively. The determination of BRR levels may enable risk assessors to utilize fetal endocrine data to help establish points of departure for quantitative risk assessments.

hero.3350216

Guerranti, C; Cau, A; Renzi, M; Badini, S; Grazioli, E; Perra, G; Focardi, SE. (2016). Phthalates and perfluorinated alkylated substances in Atlantic bluefin tuna (Thunnus thynnus) specimens from Mediterranean Sea (Sardinia,

Italy): Levels and risks for human consumption. J Environ Sci Health B 51: 1-7. http://dx.doi.org/10.1080/03601234.2016.1191886.
Atlantic blue fin tuna (Thunnus thynnus) is a species of great importance for Mediterranean Sea area, from both ecological and commercial points of view. The scientific literature reports few data on the contamination of this fish by emerging organic compounds such as perfluorinated alkylated substances(PFASs) and phthalates, being the latter never been studied in tuna. This study therefore investigated the presence of the PFASs perfluorooctane sulphonate (PFOS) and perfluoroctanoic acid (PFOA) and the phthalate di-2-ethylhexyl phthalate (DEHP), also monitored by its metabolite mono-2-ethylhexyl phthalate(MEHP), to assess both the state of contamination of Atlantic bluefin tuna specimen and the risk due to the toxicity of these compounds for human consumption. While PFOA was never found, detectable levels of PFOS (0.4-1.88ng/g), DEHP (9-14.62ng/g) and MEHP (1.5-6.30ng/g) were found. The results were elaborated relating the accumulation to the size and age of the individuals and showed a correlation between the levels of different pollutants investigated.

hero.3466597

Gyllenhammar, I; Glynn, A; Jönsson, BA; Lindh, CH; Darnerud, PO; Svensson, K; Lignell, S. (2017). Diverging temporal trends of human exposure to bisphenols and plastizisers, such as phthalates, caused by substitution of legacy EDCs? Environ Res 153: 48-54. http://dx.doi.org/10.1016/j.envres.2016.11.012.
Phthalates and phenolic substances were investigated in urine samples from first-time mothers in Uppsala, Sweden, collected between 2009 and 2014. These substances have a comparably fast metabolism and urinary metabolites are predominantly analysed. The main aim was to investigate if measures to decrease production and use of certain phthalates and bisphenol A (BPA) have resulted in decreased human exposure, and to determine if exposures to replacement chemicals have increased. Temporal trends were evaluated for metabolites (n=13) of seven phthalates, a phthalate replacer, four different bisphenols, triclosan, one organophosphate-based flame retardant, and for two pesticides. The results showed downward trends of several phthalates which are in the process of being regulated and phased out. Concomitantly, an increasing trend was seen for a metabolite of the phthalate replacer Di-iso-nonylcyclohexane 1,2-dicarboxylate (DiNCH). Bisphenol A (BPA) showed a downward trend, whereas bisphenol F, identified as one of the substitutes for BPA, showed an increasing trend. The decreasing trend of triclosan is likely due to declining use within the EU. Temporal trend studies of urine samples make it possible to investigate human exposure to rapidly metabolised substances and study how measures taken to regulate and replace problematic chemicals affect human exposure.

hero.3469436

Hadrup, N; Svingen, T; Mandrup, K; Skov, K; Pedersen, M; Frederiksen, H; Frandsen, HL; Vinggaard, AM. (2016). Juvenile Male Rats Exposed to a Low-Dose Mixture of Twenty-Seven Environmental Chemicals Display Adverse Health Effects. PLoS ONE 11: e0162027. http://dx.doi.org/10.1371/journal.pone.0162027.
Humans are exposed to a large number of environmental chemicals in their daily life, many of which are readily detectable in blood or urine. It remains uncertain if these chemicals can cause adverse health effects when present together at low doses. In this study we have tested whether a mixture of 27 chemicals administered orally to juvenile male rats for three months could leave a pathophysiological footprint. The mixture contained metals, perfluorinated compounds, PCB, dioxins, pesticides, heterocyclic amines, phthalate, PAHs and others, with a combined dose of 0.16 (Low dose), 0.47 (Mid dose) or 1.6 (High dose) mg/kg bw/day. The lowest dose was designed with the aim of obtaining plasma or urine concentrations in rats at levels approaching those observed in humans. Some single congeners were administered at doses representative of combined doses for chemical groups. With this baseline, we found effects on weight, histology and gene expression in the liver, as well as changes to the blood plasma metabolome in all exposure groups, including low-dose. Additional adverse effects were observed in the higher dosed groups, including enlarged kidneys and alterations to the metabolome. No significant effects on reproductive parameters were observed.

hero.3469432

Haines, DA; Saravanabhavan, G; Werry, K; Khoury, C. (2016). An overview of human biomonitoring of environmental chemicals in the Canadian Health Measures Survey: 2007-2019 [Review]. Int J Hyg Environ Health.

http://dx.doi.org/10.1016/j.ijheh.2016.08.002.
Human biomonitoring (HBM) is used to indicate and quantify exposure by measuring environmental chemicals, their metabolites or reaction products in biological specimens. The biomonitoring component of the Canadian Health Measures Survey (CHMS) is the most comprehensive initiative providing general population HBM data in Canada. The CHMS is an ongoing cross-sectional direct measures survey implemented in 2-year cycles. It provides nationally-representative data on health, nutritional status, environmental exposures, and related risks and protective characteristics. The survey follows a robust planning, design and sampling protocol as well as a comprehensive quality assurance and quality control regime implemented for all aspect of the survey to ensure the validity of the HBM results. HBM blood and urine data are available for CHMS cycles 1 (2007-2009), 2 (2009-2011) and 3 (2012-2013). Field collection has been completed for cycle 4 (2014-2015), with cycle 5 (2016-2017) in progress and cycle 6 planning (2018-2019) being finalized. Biomonitoring results for 279 chemicals are expected over the six cycles of the CHMS (220 in individual blood, urine or hair samples, and 59 in pooled serum samples). The chemicals include metals and trace elements, polychlorinated biphenyls (PCBs), organochlorines, flame retardants, perfluoroalkyl substances, volatile organic compounds (VOCs) and metabolites, environmental phenols, triclocarban, acrylamide, pesticides (e.g., triazines, carbamates, organophosphates, phenoxy, pyrethroids) and/or their metabolites, chlorophenols, polycyclic aromatic hydrocarbon (PAH) metabolites, phthalates and alternate plasticizer metabolites, and tobacco biomarkers. Approximately one half of the chemicals measured in individual blood and urine samples over the first three cycles were detected in more than 60% of samples. CHMS biomonitoring data have been used to establish baseline HBM concentrations in Canadians; inform public health, regulatory risk assessment and management decisions; and fulfil national and international reporting requirements. Concurrent efforts are underway in Canada to develop statistically- and risk-based concepts and tools to interpret biomonitoring data.

hero.3229679

Harley, KG; Kogut, K; Madrigal, DS; Cardenas, M; Vera, IA; Meza-Alfaro, G; She, J; Gavin, Q; Zahedi, R; Bradman, A; Eskenazi, B; Parra, KL. (2016). Reducing Phthalate, Paraben, and Phenol Exposure from Personal Care Products in Adolescent Girls: Findings from the HERMOSA Intervention Study. Environ Health Perspect 124: 1600-1607. http://dx.doi.org/10.1289/ehp.1510514.
BACKGROUND: Personal care products are a source of exposure to potentially endocrine disrupting chemicals such as phthalates, parabens, triclosan, and benzophenone-3 (BP-3) for adolescent girls.

METHODS: We enrolled 100 Latina girls in a youth-led, community-based participatory research intervention study to determine whether using personal care products whose labels stated they did not contain these chemicals for three days could lower urinary concentrations. Pre- and post-intervention urine samples were analyzed for phthalate metabolites, parabens, triclosan and BP-3 using high-performance liquid chromatography/tandem mass spectrometry.

RESULTS: Urinary concentrations of mono-ethyl phthalate (MEP) decreased by 27.4% (95% Confidence Interval (CI): -39.3, -13.2) on average over the 3 day intervention; no significant changes were seen in urinary concentrations of mono-n-butyl phthalate (MnBP) and mono-isobutyl phthalate (MiBP). Methyl and propyl paraben concentrations decreased by 43.9% (95% CI: -61.3, -18.8) and 45.4% (95% CI: -63.7, -17.9), respectively. Unexpectedly, concentrations of ethyl and butyl paraben concentrations increased, although concentrations were low overall and not detected in almost half the samples. Triclosan concentrations decreased by 35.7% (95% CI: -53.3, -11.6) and BP-3 concentrations decreased by 36.0% (95% CI: -51.0, -16.4).

DISCUSSION: This study demonstrates that techniques available to consumers, such as choosing personal care products that are labelled to be free of phthalates, parabens, triclosan, and BP-3, can reduce personal exposure to possible endocrine disrupting chemicals. Involving youth in the design and implementation of the study was key to recruitment, retention, compliance, and acceptability of the intervention.

hero.3350233

Hart, RJ. (2016). Physiological Aspects of Female Fertility: Role of the Environment, Modern Lifestyle, and Genetics [Review]. Physiol Rev 96: 873-909. http://dx.doi.org/10.1152/physrev.00023.2015.
Across the Western World there is an increasing trend to postpone childbearing. Consequently, the negative influence of age on oocyte quality may lead to a difficulty in conceiving for many couples. Furthermore,

lifestyle factors may exacerbate a couple's difficulty in conceiving due mainly to the metabolic influence of obesity; however, the negative impacts of low peripheral body fat, excessive exercise, the increasing prevalence of sexually transmitted diseases, and smoking all have significant negative effects on fertility. Other factors that impede conception are the perceived increasing prevalence of the polycystic ovary syndrome, which is further exacerbated by obesity, and the presence of uterine fibroids and endometriosis (a progressive pelvic inflammatory disorder) which are more prevalent in older women. A tendency for an earlier sexual debut and to have more sexual partners has led to an increase in sexually transmitted diseases. In addition, there are several genetic influences that may limit the number of oocytes within the ovary; consequently, by postponing attempts at childbearing, a limitation of oocyte number may become evident, whereas in previous generations with earlier conception this potentially reduced reproductive life span did not manifest in infertility. Environmental influences on reproduction are under increasing scrutiny. Although firm evidence is lacking however, dioxin exposure may be linked to endometriosis, phthalate exposure may influence ovarian reserve, and bisphenol A may interfere with oocyte development and maturation. However, chemotherapy or radiotherapy is recognized to lead to ovarian damage and predispose the woman to ovarian failure.

hero.3472927

He, Y; Wang, X; Wu, K. (2016). Evaluating Breast Cancer Risk under Exposure to Environmental Estrogen-Like Chemicals. Pol J Environ Stud 25: 2239-2249. http://dx.doi.org/10.15244/pjoes/64282.

Breast cancer is the most prevalent cancer among women in the world, with a notable increasing prevalence in recent decades. Many environmental compounds with estrogenic activity, called environmental estrogens (EEs), which are especially persistent organic pollutants, may play important roles in the occurrence and development of breast cancer and even treatment and prognosis. EE compounds, including bisphenol A, nonylphenol, phthalates, perfluorooctane sulfonate, polybrominated diphenyl ethers, dioxins, and polychlorinated biphenyls, result from industrial manufacturing and exist ubiquitously in the human environment. With the aggravation of environmental pollution, these compounds are residual in all kinds of environmental matrices - especially in industrialized countries. Humans are frequently exposed to them through various pathways, including body contact, inhalation, diet, household products, dust, and cosmetics. They have been detected in many types of human specimens. Their persistence in environmental matrices and humans has aroused global attention because of their effect on public health, especially the occurrence of breast cancer. In this review, we focus on recent research of these seven familiar EEs in industrial pollutants to provide insight into the evidence for risk of breast cancer with exposure to environmental estrogen-like chemicals and to provide clues for prevention and control of breast cancer.

hero.3469252

Herberth, G; Pierzchalski, A; Feltens, R; Bauer, M; Röder, S; Olek, S; Hinz, D; Borte, M; von Bergen, M; Lehmann, I; Group, LS. (2016). Prenatal phthalate exposure associates with low regulatory T-cell numbers and atopic dermatitis in early childhood: Results from the LINA mother-child study. J Allergy Clin Immunol. http://dx.doi.org/10.1016/j.jaci.2016.09.034.

hero.3350213

Hewlett, M; Chow, E; Aschengrau, A; Mahalingaiah, S. (2016). Prenatal Exposure to Endocrine Disruptors: A Developmental Etiology for Polycystic Ovary Syndrome. Reproductive Sciences. http://dx.doi.org/10.1177/1933719116654992.

Polycystic ovary syndrome (PCOS) is one of the most common and complex endocrinopathies among reproductive-age women. Polycystic ovary syndrome is characterized by symptomatology of oligomenorrhea and androgen excess, with or without presence of polycystic ovarian morphology. The etiology of PCOS is multifactorial, including genetic and environmental components. It has been previously established that prenatal androgen exposure results in a PCOS phenotype in experimental animal models and epidemiologic human studies. Investigators hypothesize that prenatal exposure to endocrine-disrupting chemicals (EDCs) may contribute to PCOS development. This review examines the emerging research investigating prenatal exposure to 3 major classes of EDCs-bisphenol A (BPA), phthalates, and androgenic EDCs-and the development of PCOS and/or PCOS-related abnormalities in humans and animal models. Highlights of this review are as follows: (1) In rodent studies, maternal BPA exposure alters postnatal development and sexual

maturation;, (2) gestational exposure to dibutyl phthalate and di(2-ethylhexyl)phthalate results in polycystic ovaries and a hormonal profile similar to PCOS; and (3) androgenic EDCs, nicotine and 3,4,4'-trichlorocarbanilide, create a hyperandrogenic fetal environment and may pose a potential concern. In summary, prenatal exposure to EDCs may contribute to the altered fetal programming hypothesis and explain the significant variability in severity and presentation.

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Ho, SM; Cheong, A; Adgent, MA; Veevers, J; Suen, AA; Tam, NN; Leung, YK; Jefferson, WN; Williams, CJ. (2016). Environmental factors, epigenetics, and developmental origin of reproductive disorders. Reprod Toxicol. http://dx.doi.org/10.1016/j.reprotox.2016.07.011.

Sex-specific differentiation, development, and function of the reproductive system are largely dependent on steroid hormones. For this reason, developmental exposure to estrogenic and anti-androgenic endocrine disrupting chemicals (EDCs) is associated with reproductive dysfunction in adulthood. Human data in support of "Developmental Origins of Health and Disease" (DOHaD) comes from multigenerational studies on offspring of diethylstilbestrol-exposed mothers/grandmothers. Animal data indicate that ovarian reserve, female cycling, adult uterine abnormalities, sperm quality, prostate disease, and mating behavior are susceptible to DOHaD effects induced by EDCs such as bisphenol A, genistein, diethylstilbestrol, p,p'-dichlorodiphenyl-dichloroethylene, phthalates, and polyaromatic hydrocarbons. Mechanisms underlying these EDC effects include direct mimicry of sex steroids or morphogens and interference with epigenomic sculpting during cell and tissue differentiation. Exposure to EDCs is associated with abnormal DNA methylation and other epigenetic modifications, as well as altered expression of genes important for development and function of reproductive tissues. Here we review the literature exploring the connections between developmental exposure to EDCs and adult reproductive dysfunction, and the mechanisms underlying these effects.

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Hoepner, LA; Whyatt, RM; Widen, EM; Hassoun, A; Oberfield, SE; Mueller, NT; Diaz, D; Calafat, AM; Perera, FP; Rundle, AG. (2016). Bisphenol A and Adiposity in an Inner-City Birth Cohort. Environ Health Perspect 124: 1644-1650. http://dx.doi.org/10.1289/EHP205.

BACKGROUND: Early-life exposure to the endocrine disruptor bisphenol A (BPA) may contribute to the development of obesity. Prospective evidence in humans on this topic is limited.

OBJECTIVES: We examined prenatal and early-childhood BPA exposures in relation to childhood measures of adiposity in the Columbia Center for Children's Environmental Health (CCCEH) New York City birth cohort.

METHODS: BPA concentrations were measured in prenatal (n = 375) and child ages 3 (n = 408) and 5 years (n = 518) spot urine samples. Childhood anthropometric and bioelectrical impedance outcomes included body mass index z-scores (BMIZ) at 5 and 7 years, and fat mass index (FMI), percent body fat (%BF), and waist circumference (WC) at 7 years. Associations were evaluated using multiple linear regression with continuous and tertile BPA concentrations.

RESULTS: Prenatal urinary BPA concentrations were positively associated with child age 7 FMI (β = 0.31 kg/m2; 95% CI: 0.01, 0.60, p = 0.04), %BF (β = 0.79; 95% CI: 0.03, 1.55, p = 0.04), and WC (β = 1.29 cm; 95% CI: 0.29, 2.30, p = 0.01), but not BMIZ, or change in BMIZ between ages 5 and 7 years (all p-values > 0.1). FMI results were sex-specific. Child urinary BPA concentrations were not associated with child anthropometric outcomes (all p-values > 0.05).

CONCLUSIONS: Analyses of the CCCEH longitudinal birth cohort found associations between prenatal urinary BPA concentrations and FMI, %BF, and WC. Our results suggest that prenatal BPA exposure may contribute to developmental origins of adiposity. These findings are consistent with several prior studies, raising concern about the pervasiveness of BPA.

CITATION: Hoepner LA, Whyatt RM, Widen EM, Hassoun A, Oberfield SE, Mueller NT, Diaz D, Calafat AM, Perera FP, Rundle AG. 2016. Bisphenol A and adiposity in an inner-city birth cohort. Environ Health Perspect 124:1644-1650; http://dx.doi.org/10.1289/EHP205.

hero.3466577

Holland, N; Huen, K; Tran, V; Street, K; Nguyen, B; Bradman, A; Eskenazi, B. (2016). Urinary Phthalate Metabolites and Biomarkers of Oxidative Stress in a Mexican-American Cohort: Variability in Early and Late Pregnancy. 4.

http://dx.doi.org/10.3390/toxics4010007.

People are exposed to phthalates through their wide use as plasticizers and in personal care products. Many phthalates are endocrine disruptors and have been associated with adverse health outcomes. However, knowledge gaps exist in understanding the molecular mechanisms associated with the effects of exposure in early and late pregnancy. In this study, we examined the relationship of eleven urinary phthalate metabolites with isoprostane, an established marker of oxidative stress, among pregnant Mexican-American women from an agricultural cohort. Isoprostane levels were on average 20% higher at 26 weeks than at 13 weeks of pregnancy. Urinary phthalate metabolite concentrations suggested relatively consistent phthalate exposures over pregnancy. The relationship between phthalate metabolite concentrations and isoprostane levels was significant for the sum of di-2-ethylhexyl phthalate and the sum of high molecular weight metabolites with the exception of monobenzyl phthalate, which was not associated with oxidative stress at either time point. In contrast, low molecular weight metabolite concentrations were not associated with isoprostane at 13 weeks, but this relationship became stronger later in pregnancy (p-value = 0.009 for the sum of low molecular weight metabolites). Our findings suggest that prenatal exposure to phthalates may influence oxidative stress, which is consistent with their relationship with obesity and other adverse health outcomes.

hero.3469526

Houten, SM; Chen, J; Belpoggi, F; Manservisi, F; Sánchez-Guijo, A; Wudy, SA; Teitelbaum, SL. (2016). Changes in the Metabolome in Response to Low-Dose Exposure to Environmental Chemicals Used in Personal Care Products during Different Windows of Susceptibility. PLoS ONE 11: e0159919. http://dx.doi.org/10.1371/journal.pone.0159919.

The consequences of ubiquitous exposure to environmental chemicals remain poorly defined. Non-targeted metabolomic profiling is an emerging method to identify biomarkers of the physiological response to such exposures. We investigated the effect of three commonly used ingredients in personal care products, diethyl phthalate (DEP), methylparaben (MPB) and triclosan (TCS), on the blood metabolome of female Sprague-Dawley rats. Animals were treated with low levels of these chemicals comparable to human exposures during prepubertal and pubertal windows as well as chronically from birth to adulthood. Non-targeted metabolomic profiling revealed that most of the variation in the metabolites was associated with developmental stage. The low-dose exposure to DEP, MPB and TCS had a relatively small, but detectable impact on the metabolome. Multiple metabolites that were affected by chemical exposure belonged to the same biochemical pathways including phenol sulfonation and metabolism of pyruvate, lyso-plasmalogens, unsaturated fatty acids and serotonin. Changes in phenol sulfonation and pyruvate metabolism were most pronounced in rats exposed to DEP during the prepubertal period. Our metabolomics analysis demonstrates that human level exposure to personal care product ingredients has detectable effects on the rat metabolome. We highlight specific pathways such as sulfonation that warrant further study.

hero.3466591

Howdeshell, KL; Hotchkiss, AK; Gray, LE. (2016). Cumulative effects of antiandrogenic chemical mixtures and their relevance to human health risk assessment [Review]. Int J Hyg Environ Health. http://dx.doi.org/10.1016/j.ijheh.2016.11.007.

Toxicological studies of defined chemical mixtures assist human health risk assessment by establishing how chemicals interact with one another to induce an effect. This paper reviews how antiandrogenic chemical mixtures can alter reproductive tract development in rats with a focus on the reproductive toxicant phthalates. The reviewed studies compare observed mixture data to mathematical mixture model predictions based on dose addition or response addition to determine how the individual chemicals in a mixture interact (e.g., additive, greater, or less than additive). Phthalate mixtures were observed to act in a dose additive manner based on the relative potency of the individual phthalates to suppress fetal testosterone production. Similar dose additive effects have been reported for mixtures of phthalates with antiandrogenic pesticides of differing mechanisms of action. Overall, data from these phthalate experiments in rats can be used in conjunction with human biomonitoring data to determine individual hazard indices, and recent cumulative risk assessments in humans indicate an excess risk to antiandrogenic chemical mixtures that include phthalates only or phthalates in combination with other antiandrogenic chemicals.

hero.3052883

Howdeshell, KL; Rider, CV; Wilson, VS; Furr, JR; Lambright, CR; Gray, LE. (2015). Dose addition models based on biologically relevant reductions in fetal testosterone accurately predict postnatal reproductive tract alterations by a phthalate mixture in rats. Toxicol Sci 148: 488-502. http://dx.doi.org/10.1093/toxsci/kfv196.
Challenges in cumulative risk assessment of anti-androgenic phthalate mixtures include a lack of data on all the individual phthalates and difficulty determining the biological relevance of reduction in fetal testosterone (T) on postnatal development. The objectives of the current study were 2-fold: (1) to test whether a mixture model of dose addition based on the fetal T production data of individual phthalates would predict the effects of a 5 phthalate mixture on androgen-sensitive postnatal male reproductive tract development, and (2) to determine the biological relevance of the reductions in fetal T to induce abnormal postnatal reproductive tract development using data from the mixture study. We administered a dose range of the mixture (60, 40, 20, 10, and 5% of the top dose used in the previous fetal T production study consisting of 300 mg/kg per chemical of benzyl butyl (BBP), di(n)butyl (DBP), diethyl hexyl phthalate (DEHP), di-isobutyl phthalate (DiBP), and 100 mg dipentyl (DPP) phthalate/kg; the individual phthalates were present in equipotent doses based on their ability to reduce fetal T production) via gavage to Sprague Dawley rat dams on GD8-postnatal day 3. We compared observed mixture responses to predictions of dose addition based on the previously published potencies of the individual phthalates to reduce fetal T production relative to a reference chemical and published postnatal data for the reference chemical (called DAref). In addition, we predicted DA (called DAall) and response addition (RA) based on logistic regression analysis of all 5 individual phthalates when complete data were available. DA ref and DA all accurately predicted the observed mixture effect for 11 of 14 endpoints. Furthermore, reproductive tract malformations were seen in 17-100% of F1 males when fetal T production was reduced by about 25-72%, respectively.

hero.3469424

Hsu, JY; Hsu, JF; Chen, YR; Shih, CL; Hsu, YS; Chen, YJ; Tsai, SH; Liao, PC. (2016). Urinary exposure marker discovery for toxicants using ultra-high pressure liquid chromatography coupled with Orbitrap high resolution mass spectrometry and three untargeted metabolomics approaches. Anal Chim Acta 939: 73-83. http://dx.doi.org/10.1016/j.aca.2016.07.032.
Human biomonitoring is the assessment of actual internal contamination of chemicals by measuring exposure markers, chemicals or their metabolites, in human urine, blood, serum, and other body fluids. However, the metabolism of chemicals within an organism is extremely complex. Therefore, the identification of metabolites is often difficult and laborious. Several untargeted metabolomics methods have been developed to perform objective searching/filtering of accurate-mass-based LC-MS data to facilitate metabolite identification. In this study, three metabolomics data processing approaches were used for chemical exposure marker discovery in urine with an LTQ-Orbitrap high-resolution mass spectrometry (HRMS) dataset; di-isononyl phthalate (DINP) was used as an example. The data processing techniques included the SMAIT, mass defect filtering (MDF), and XCMS Online. Sixteen, 83, and 139 probable DINP metabolite signals were obtained using the SMAIT, MDF, and XCMS procedures, respectively. Fourteen probable metabolite signals mined simultaneously by the three metabolomics approaches were confirmed as DINP metabolites by structural information provided by LC-MS/MS. Among them, 13 probable metabolite signals were validated as exposure-related markers in a rat model. Six (m/z 319.155, 361.127, 373.126, 389.157, 437.112 and 443.130) of the 13 exposure-related DINP metabolite signals have not previously been reported in the literature. Our data indicate that SMAIT provided an efficient method to discover effectively and systematically urinary exposure markers of toxicant. The DINP metabolism information can provide valuable information for further investigations of DINP toxicity, toxicokinetics, exposure assessment, and human health effects.

hero.3350368

Hsu, PC; Kuo, YT; Leon Guo, Y; Chen, J. R.; Tsai, SS; Chao, HR; Teng, YN; Pan, MH. (2016). The adverse effects of low-dose exposure to Di(2-ethylhexyl) phthalate during adolescence on sperm function in adult rats. Environ Toxicol 31: 706-712. http://dx.doi.org/10.1002/tox.22083.
Di(2-ethylhexyl) phthalate (DEHP) is the most crucial phthalate derivative added to polyvinyl chloride as a plasticizer. This study examined the effects of low-dose exposure to DEHP during adolescence on sperm function in adult rats. The male rats were daily gavaged with 30, 100, 300, and 1000 μg kg(-1) of DEHP or corn oil from postnatal day (PND) 42 until PND 105. The selection of DEHP doses ranged from the mean

daily intake by the normal-population exposure levels to no-observed-adverse-effect level of DEHP for the endpoints evaluated until adulthood. Significant increases in the percentage of sperm with tail abnormality, tendency for sperm DNA fragmentation index (DFI) and percentage of sperm with DFI were found in those exposed to 100, 300, and 1000 μg kg(-1) (P < 0.05). We observed a significant increase of hydrogen peroxide (H2 O2) generation in the sperm of the 1000 μg kg(-1) group compared with the control group (P < 0.05). The excessive production of sperm H2 O2 coincided with an increase in sperm DFI. In this study, the lowest-observed-adverse-effect level for sperm toxicity was considered to be 100 μg DEHP/kg/day in sperm morphology and chromatin DNA damage. Further research is necessary to clarify the mechanisms of DEHP-related sperm ROS generation on sperm DNA damage. 2014 Wiley Periodicals, Inc. Environ Toxicol 31: 706-712, 2016.

hero.3466582

Hu, W; Zhang, Y; Huang, B; Teng, Y. (2017). Soil environmental quality in greenhouse vegetable production systems in eastern China: Current status and management strategies. Chemosphere 170: 183-195. http://dx.doi.org/10.1016/j.chemosphere.2016.12.047.

Greenhouse vegetable production (GVP) has become an important source of public vegetable consumption and farmers' income in China. However, various pollutants can be accumulated in GVP soils due to the high cropping index, large agricultural input, and closed environment. Ecological toxicity caused by excessive pollutants' accumulation can then lead to serious health risks. This paper was aimed to systematically review the current status of soil environmental quality, analyze their impact factors, and consequently to propose integrated management strategies for GVP systems. Results indicated a decrease in soil pH, soil salinization, and nutrients imbalance in GVP soils. Fungicides, remaining nutrients, antibiotics, heavy metals, and phthalate esters were main pollutants accumulating in GVP soils comparing to surrounding open field soils. Degradation of soil ecological function, accumulation of major pollutants in vegetables, deterioration of neighboring water bodies, and potential human health risks has occurred due to the changes of soil properties and accumulation of pollutants such as heavy metals and fungicides in soils. Four dominant factors were identified leading to the above-mentioned issues including heavy application of agricultural inputs, outmoded planting styles with poor environmental protection awareness, old-fashion regulations, unreasonable standards, and ineffective supervisory management. To guarantee a sustainable GVP development, several strategies were suggested to protect and improve soil environmental quality. Implementation of various strategies not only requires the concerted efforts among different stakeholders, but also the whole lifecycle assessment throughout the GVP processes as well as effective enforcement of policies, laws, and regulations.

hero.3479523

Hu, X; Gu, Y; Huang, W; Yin, D. (2016). Phthalate monoesters as markers of phthalate contamination in wild marine organisms. Environ Pollut 218: 410-418. http://dx.doi.org/10.1016/j.envpol.2016.07.020.

The level of phthalate esters (PAEs) alone is not considered to be a sufficient indicator of PAE pollution due to the quick metabolism of PAEs in the biota. The primary metabolites of PAEs, monoalkyl phthalate esters (MPEs), may also be an important indicator. However, PAE metabolism has scarcely been documented in wild marine organisms. We analysed five PAEs [dimethyl phthalate (DMP), diethyl phthalate (DEP), di-n-butyl phthalate (DBP), di(2-ethylhexyl) phthalate (DEHP), and di-n-octyl phthalate (DNOP)] and their corresponding MPEs [mono-methyl phthalate (MMP), mono-ethyl phthalate (MEP), mono-n-butyl phthalate (MBP), mono-2-ethylhexyl phthalate (MEHP), and mono-n-octyl phthalate (MNOP)] in 95 wild aquatic marine samples (including fish, prawns and molluscs) collected from the Yangtze River Delta area of the East China Sea. The species-dependent distribution of these compounds was associated with the food habits, living patterns and trophic levels of the biota. Slightly higher levels of hydrophobic PAEs (DBP and DEHP, logKOW 4.27 and 7.33, respectively) were observed in fish species consuming benthic organisms or in demersal fish species, suggesting the importance of benthic organisms and sediment. Trophic dilution of both PAEs and MPEs implies further metabolic transformation at higher trophic levels. MPE tissue distributions in fish demonstrate that the highest concentrations were always observed in bile. Metabolism via the kidney and gill is a probable main way for the relatively less hydrophobic MPEs (logKOW=<4.73, from MMP to MEHP), whereas metabolism via the liver is likely the main way for the most hydrophobic MNOP (logKOW 5.22). Generally, higher detection frequencies of MPEs were observed than those of parent PAEs. Significant liner

correlations were observed between the levels of short-branched (carbon atom per chain=<4) MPEs and the sum of PAEs and MPEs (n=95, p<0.01), demonstrating that short-branched MPEs can be used as biomarkers of exposure to quantitatively reflect parent PAE contamination in wild marine organisms.

hero.3468001

Huang, D, i; Xiu, G; Li, M; Hua, X, in; Long, Y. (2017). Surface components of PM2.5 during clear and hazy days in Shanghai by ToF-SIMS. Atmos Environ 148: 175-181. http://dx.doi.org/10.1016/j.atmosenv.2016.10.036.
The compositions of atmospheric particles change greatly on hazy days and could threaten human health. In this study, fine mode particles (PM2.5) were collected and divided according to hazy and non hazy days in Shanghai from December 8th, 2015 to January 12th, 2016. Versatile ToF-SIMS was performed on the samples to reveal chemical information from the surface of PM2.5. Normalized intensities of Na, Mn, K, V, Al, Fe, Ca, Ti, Cl, NOx, and ammonia were higher on clear days while peak intensities of detected bromine and sulfur-contained species were much higher on hazy days. Some hazardous species (Pb, Cr, Ni, As, CHS, SO2) and high-mass aromatic hydrocarbon fractions could only be detected by ToF-SIMS from PM2.5 collected on hazy days. Comparison of metallic elements and phthalates implied that haze pollution in Shanghai was mainly the mixing of coal combustion with vehicle emission. In addition, comparison of different haze pollution was also exhibited. Some nitrogen-containing organic compounds were detected only from PM2.5 of December 15th, and ToF-SIMS ion signals of N2H5+ NH4+, CN-, NO2- and NO3- from PM2.5 of December 15th were much more intense, compared with PM2.5 collected on December 25th. (C) 2016 Elsevier Ltd. All rights reserved.

hero.3466596

Huang, HB; Pan, WH; Chang, JW; Chiang, HC; Guo, YL; Jaakkola, JJ; Huang, PC. (2017). Does exposure to phthalates influence thyroid function and growth hormone homeostasis? The Taiwan Environmental Survey for Toxicants (TEST) 2013. Environ Res 153: 63-72. http://dx.doi.org/10.1016/j.envres.2016.11.014.
BACKGROUND: Previous epidemiologic and toxicological studies provide some inconsistent evidence that exposure to phthalates may affect thyroid function and growth hormone homeostasis.

OBJECTIVE: To assess the relations between exposure to phthalates and indicators of thyroid function and growth hormone homeostasis disturbances both among adults and minors.

METHODS: We conducted a population-based cross-sectional study of 279 Taiwanese adults (18 years old) and 79 minors (<18 years old) in 2013. Exposure assessment was based on urinary biomarkers, 11 phthalate metabolites measured by using online liquid chromatography/tandem mass spectrometry. Indicators of thyroid function included serum levels of thyroxine (T4), free T4, triiodothyronine, thyroid-stimulating hormone, and thyroxine-binding globulin (TBG). Growth hormone homeostasis was measured as the serum levels of insulin-like growth factor 1 (IGF-1) and insulin-like growth factor binding protein 3 (IGFBP3). We applied multivariate linear regression models to examine these associations after adjusting for covariates.

RESULTS: Among adults, serum T4 levels were negatively associated with urinary mono-(2-ethyl-5-hydroxyhexyl) phthalate (β=-0.028, P=0.043) and the sum of urinary di-(2-ethylhexyl) phthalate (DEHP) metabolite (β=-0.045, P=0.017) levels. Free T4 levels were negatively associated with urinary mono-ethylhexyl phthalate (MEHP) (β=-0.013, P=0.042) and mono-(2-ethyl-5-oxohexyl) phthalate (β=-0.030, P=0.003) levels, but positively associated with urinary monoethyl phthalate (β=0.014, P=0.037) after adjustment for age, BMI, gender, urinary creatinine levels, and TBG levels. Postive associations between urinary MEHP levels and IGF-1 levels (β=0.033, P=0.006) were observed. Among minors, free T4 was positively associated with urinary mono benzyl phthalate levels (β=0.044, P=0.001), and IGF-1 levels were negatively associated with the sum of urinary DEHP metabolite levels (β=-0.166, P=0.041) after adjustment for significant covariance and IGFBP3.

CONCLUSIONS: Our results are consistent with the hypothesis that exposure to phthalates influences thyroid function and growth hormone homeostasis.

hero.3469529

Huang, PC; Tsai, CH; Liang, WY; Li, SS; Huang, HB; Kuo, PL. (2016). Early Phthalates Exposure in Pregnant Women Is Associated with Alteration of Thyroid Hormones. PLoS ONE 11: e0159398. http://dx.doi.org/10.1371/journal.pone.0159398.
INTRODUCTION: Previous studies revealed that phthalate exposure could alter thyroid

hormones during the last trimester of pregnancy. However, thyroid hormones are crucial for fetal development during the first trimester. We aimed to clarify the effect of phthalate exposure on thyroid hormones during early pregnancy.

METHOD: We recruited 97 pregnant women who were offered an amniocentesis during the early trimester from an obstetrics clinic in southern Taiwan from 2013 to 2014. After signing an informed consent form, we collected amniotic fluid and urine samples from pregnant women to analyze 11 metabolites, including mono-ethyl phthalate (MEP), mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP), mono-(2-ethylhexyl) phthalate (MEHP), mono-butyl phthalate (MnBP), of 9 phthalates using liquid chromatography/ tandem mass spectrometry. We collected blood samples from each subject to analyze serum thyroid hormones including thyroxine (T4), free T4, and thyroid-binding globulin (TBG).

RESULTS: Three phthalate metabolites were discovered to be >80% in the urine samples of the pregnant women: MEP (88%), MnBP (81%) and MECPP (86%). Median MnBP and MECPP levels in pregnant Taiwanese women were 21.5 and 17.6 μg/g-creatinine, respectively, that decreased after the 2011 Taiwan DEHP scandal. Results of principal component analysis suggested two major sources (DEHP and other phthalates) of phthalates exposure in pregnant women. After adjusting for age, gestational age, TBG, urinary creatinine, and other phthalate metabolites, we found a significantly negative association between urinary MnBP levels and serum T4 (β = -5.41; p-value = 0.012; n = 97) in pregnant women using Bonferroni correction.

CONCLUSION: We observed a potential change in the thyroid hormones of pregnant women during early pregnancy after DnBP exposure. Additional study is necessitated to clarify these associations.

hero.3479511

Hunt, PA; Sathyanarayana, S; Fowler, PA; Trasande, L. (2016). Female Reproductive Disorders, Diseases, and Costs of Exposure to Endocrine Disrupting Chemicals in the European Union. J Clin Endocrinol Metab 101: 1562-1570. http://dx.doi.org/10.1210/jc.2015-2873.

We estimated the economic costs of female reproductive disorders attributable to endocrine disrupting chemical exposures. These may contribute substantially to fibroids and endometriosis, costing nearly 1.5 billion annually.

hero.3350217

Huo, CY; Liu, LY; Zhang, ZF; Ma, WL; Song, WW; Li, HL; Li, WL; Kannan, K; Wu, YK; Han, YM; Peng, ZX; Li, YF. (2016). Phthalate Esters in Indoor Window Films in a Northeastern Chinese Urban Center: Film Growth and Implications for Human Exposure. Environ Sci Technol 50: 7743-7751. http://dx.doi.org/10.1021/acs.est.5b06371.

Indoor window film samples were collected in buildings during 2014-2015 for the determination of six phthalate diesters (PAEs). Linear regression analysis suggested that the film mass was positively and significantly correlated with the duration of film growth (from 7 to 77 days). PAEs were detected in all window film samples (n = 64). For all the samples with growth days ranged from 7 to 77 days, the median concentrations of total six PAEs (6PAEs) in winter and summer window film samples were 9900 ng/m(2) film (2000 μg/g film) and 4700 ng/m(2) film (650 μg/g film), respectively. Among PAEs analyzed, di-2-ethyl-hexyl phthalate (DEHP) was the major compound (71 9.7%), followed by di-n-butyl phthalate (DBP; 20 7.4%) and diisobutyl phthalate (DiBP; 5.1 2.2%). Positive correlations among PAEs suggested their common sources in the window film samples. Room temperature and relative humidity were negatively and significantly correlated with PAEs concentations (in ng/m(2)). Poor ventilation in cold winter in Noreastern China significantly influenced the concentrations of PAEs in window film which suggested higher inhalation exposure dose in winter. The median hazard quotient (HQ) values from PAEs exposure were below 1, suggesting that the intake of PAEs via three exposure pathways was considered as acceptable.

hero.3469546 REVIEW

Huo, L; Lyons, J; Magliano, DJ. (2016). Infectious and Environmental Influences on the Obesity Epidemic [Review]. 5: 375-382. http://dx.doi.org/10.1007/s13679-016-0224-9.

Over the last two decades, the prevalence of obesity has increased rapidly. While it is intuitively appealing to believe that the causes of obesity are manifestly related to excess dietary intake, combined with a reduced expenditure of energy via a decrease in physical activity, it is also been noted that the evidence for these as the sole causes of the obesity epidemic is incomplete. This has led to the search for other causes of obesity,

particularly those which stem from the environment we live in. This review will explore two putative causes of obesity: infections and environmental pollutants. It will focus on the key human infection associated with obesity-human adenovirus 36 (Ad36) and will discuss several environmental pollutants which have been postulated to be involved in the development of obesity: bisphenol A, phthalates and persistent organic pollutants. For each of these, the epidemiology and biological mechanisms underpinning the association of these agents with obesity will be reviewed.

hero.3008865

Jalbert, I; Golebiowski, B. (2015). Environmental aeroallergens and allergic rhino-conjunctivitis [Review]. Curr Opin Allergy Clin Immunol 15: 476-481. http://dx.doi.org/10.1097/ACI.0000000000000205.
PURPOSE OF REVIEW: The rising prevalence of allergy and of allergic rhino-conjunctivitis is associated with changes in modern lifestyle. The current period of rapid development and consequent urbanization and migration, coupled with changes in climate, is facilitating a growth in rates of allergy.

RECENT FINDINGS: Alterations to indoor and outdoor environments resulting from urbanization, industrialization, and climate change have significant implications for the prevalence and management of allergic rhino-conjunctivitis. Rising temperatures, precipitation and more extreme weather enable longer pollen seasons and greater viability of indoor and outdoor moulds and result in increased exposure to (and allergenic potential of) these aeroallergens. Outdoor air pollution is a major risk factor for rhino-conjunctivitis; key contributors are fuel combustion and dust storms because of changes in land-use and development. Further studies are needed to recognize and understand sources of indoor pollution including phthalates.

SUMMARY: A better understanding of the role of environmental aeroallergens in allergic rhino-conjunctivitis is important to aid future management of allergic conjunctivitis. Strategies such as region-specific modelling of aeroallergens (pollens, air pollution) are required to predict and thus prevent exposure and to better inform appropriate childhood exposure and minimize lifelong effects.

hero.3469326

James-Todd, TM; Meeker, JD; Huang, T; Hauser, R; Ferguson, KK; Rich-Edwards, JW; Mcelrath, TF; Seely, EW. (2016). Pregnancy urinary phthalate metabolite concentrations and gestational diabetes risk factors. Environ Int 96: 118-126. http://dx.doi.org/10.1016/j.envint.2016.09.009.
BACKGROUND: Epidemiologic studies suggest phthalate metabolite concentrations are associated with type 2 diabetes. GDM is a strong risk factor for type 2 diabetes. Little is known about phthalates and GDM risk factors (i.e. 1st trimester body mass index (BMI), gestational weight gain (GWG), and 2nd trimester glucose levels).

METHODS: A total of 350 women participating in Lifecodes pregnancy cohort (Boston, MA), delivered at term and had pregnancy urinary phthalate metabolite concentrations. Nine specific gravity-adjusted urinary phthalate metabolites were evaluated. General linear regression was used to assess associations between quartiles of phthalate metabolites and continuous 1st trimester BMI and late 2nd trimester blood glucose. Linear mixed models were used for total GWG. Multivariable logistic regression was used for phthalate concentrations and categorized GWG and impaired glucose tolerance defined as glucose140mg/dL based on a 50-gram glucose load test. Models were adjusted for potential confounders.

RESULTS: There were no associations between 1st trimester urinary phthalate metabolite concentrations and 1st trimester BMI. Mono-ethyl phthalate concentrations averaged across pregnancy were associated with a 2.17 increased odds of excessive GWG (95% CI: 0.98, 4.79). Second trimester mono-ethyl phthalate was associated with increased odds of impaired glucose tolerance (adj. OR: 7.18; 95% CI: 1.97, 26.15). A summary measure of di-2-ethylhexyl phthalate metabolite concentrations were inversely associated with impaired glucose tolerance (adj. OR: 0.25; adj. 95% CI: 0.08, 0.85).

CONCLUSIONS: Higher exposure to mono-ethyl phthalate, a metabolite of the parent compound of di-ethyl phthalate, may be associated with excessive GWG and impaired glucose tolerance; higher di-2-ethylhexyl phthalate was associated with reduced odds of impaired glucose tolerance.

hero.3469570

Jang, S; Ji, K. (2015). Effect of chronic exposure to two components of Tritan copolyester on Daphnia magna, Moina macrocopa, and Oryzias latipes, and potential mechanisms of endocrine disruption using H295R cells.

Ecotoxicology 24: 1906-1914. http://dx.doi.org/10.1007/s10646-015-1526-5.
Tritan copolyester is a novel plastic form from Eastman Company utilizing three main monomers, 1,4-cyclohexanedimethanol (CHDM), dimethyl terephthalate (DMT), and 2,2,4,4-tetramethyl-1,3-cyclobutanediol. Despite Tritan has been widely applied for plastic bottles, the effects of long-term exposure to these compounds have seldom been investigated. We investigated chronic effects and endocrine disruption potential of CHDM and terephthalic acid (TPA), main mammalian metabolite formed from DMT, using crustacean Daphnia magna and Moina macrocopa, and freshwater fish (Oryzias latipes). The effects on sex hormone balance and the associated mechanisms were also investigated by use of H295R cells. In chronic toxicity test, D. magna showed significant decrease in reproduction (number of young per female) after exposure to 10 mg/L TPA. In early life stage exposure using O. latipes, significant decrease of juvenile survival and weight were observed in fish exposed to 10 mg/L and 1 mg/L CHDM, respectively. Expressions of vtg2 mRNA in fish exposed to CHDM and those of cyp19b, star, cyp17, and cyp19a mRNAs in fish exposed to TPA were significantly up-regulated. The results of H295R cell assay also showed that both chemicals at high concentrations could alter sex hormone production in steroidogenic pathway. The effective concentrations of the tested compounds were several orders of magnitude greater than the concentrations can be detected in ambient waters. Further in vivo and in vitro studies will be needed to investigate the effect of co-polymer on endocrine disruption.

hero.3455186 REVIEW

Jeddi, MZ; Janani, L; Memari, AH; Akhondzadeh, S; Yunesian, M. (2016). The role of phthalate esters in autism development: A systematic review [Review]. Environ Res 151: 493-504. http://dx.doi.org/10.1016/j.envres.2016.08.021.

BACKGROUND: Available evidence implicates environmental factors in the pathogenesis of autism spectrum disorders (ASD). However, the role of specific environmental chemicals such as phthalate esters that influence ASD risk remains elusive. This paper systematically reviews published evidences on association between prenatal and/or childhood exposure to phthalate and ASD.

METHODS: Studies pertaining to systematic literature search from Scopus, PubMed, PsycInfo and Web of Science prior to December 2015 were identified. The authors included studies which assessed the effect of exposure to phthalates on occurrence of ASD. This comprehensive bibliographic search identified five independent studies. Each eligible paper was summarized with respect to its methods and results with particular attention to study design and exposure assessment. Because of the heterogeneity in the type of included studies, different methods of assessing exposure to phthalates and the use of different statistics for summarizing the results, meta-analysis could not be used to combine the results of included studies.

RESULTS: The results of this systematic review have revealed the limited number of studies conducted and assessed phthalate exposure. Seven studies were regarded as relevant to the objectives of this review. Two of them did not measure phthalate exposure directly and did not result in quantitative results. Out of the five studies in which phthalate exposure was mainly measured by the examining biomarkers in biological samples, two were cohort studies (one with positive results and another one with not clear association). Among the three case control studies, two of them showed a significant relation between exposure to phthalate and ASD and the last case control study had negative results. Indeed, this case control studies showed a compromised phthalate metabolite glucuronidation pathway, as a probable explanation of mechanism of the relation between phthalate exposure and ASD.

CONCLUSIONS: This review reveals evidence showing a connection between exposure to phthalates and ASD. Nevertheless, further research is needed with appropriate attention to exposure assessment and relevant pre and post-natal cofounders.

hero.3454705

Jeddi, MZ; Rastkari, N; Ahmadkhaniha, R; Yunesian, M. (2016). Endocrine disruptor phthalates in bottled water: daily exposure and health risk assessment in pregnant and lactating women. Environ Monit Assess 188: 534. http://dx.doi.org/10.1007/s10661-016-5502-1.

Over the last decade, the consumption of water bottled in polyethylene terephthalate (PET) has considerably increased, raising concerns over water quality and packaged materials. This study aims to investigate the levels of the anti-androgenic phthalates including bis-(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), and benzyl butyl phthalate (BBP), in bottled water and its corresponding health risks in pregnant and

lactating women. The phthalate levels were measured in six different brands of bottled water exposed to temperatures ranging between -18 and 40C and sunlight for 45days. The phthalate was quantified using the gas chromatography-mass spectrometry (GC-MS). In addition, the non-carcinogenic effects were assessed using hazard quotient (HQ) approach, and cumulative health risk assessment was performed on the basis of hazard index (HI) calculation. In order to assess the carcinogenic risk due to the possible carcinogen DEHP (group 2B), the excess lifetime cancer risk (ELCR) was used. DEHP and DBP contaminants were detected at different storage conditions in all of the bottled water samples during the storage time. BBP was only detected at high temperature (25C) and outdoor conditions. The maximum concentrations of all phthalates were observed when water samples were kept at 40C. In contrast, storage at freezing conditions had no significant effect on the concentration level of all phthalates. The estimated intake by women was between 0.0021μg/kg/day for BBP and 0.07μg/kg/day for DEHP. The highest HQ for phthalate intake via bottled water consumption was much lower than 1 (HQ<0.004), which implies that adverse effects are very unlikely to occur. The execution of a cumulative risk assessment for combined phthalate exposure demonstrated that the HIs for anti-androgenic effect were lower than 1 in all of the conditions. Furthermore, ELCR for DEHP based on the highest detected level was found to be less than 10(-6), which is considered acceptable. Our results prove that the levels of phthalates in bottled water are not a health concern for pregnant and lactating women. Consequently, PET-bottled water is not a major contributor to phthalate intake for most individuals.

hero.3469373

Jemimah Naine, S; Subathra Devi, C; Mohanasrinivasan, V; George Priya Doss, C. (2016). Bioactivity of Marine Streptomyces sp. VITJS4: Interactions of Cytotoxic Phthalate Derivatives with Human Topoisomerase II α: An In Silico Molecular Docking Analysis. Interdisciplinary Sciences: Computational Life Sciences. http://dx.doi.org/10.1007/s12539-016-0187-2.

Despite clinical advances in antimicrobial and anticancer therapy, there is an urge for the search of new bioactive compounds. In the present study, previously isolated Streptomyces sp. VITJS4 strain (NCIM No. 5574) (ACC No: JQ234978.1) crude extract tested for antibacterial activity showed a broad spectrum at the concentration of 20mg/mL against pathogens. The antioxidant potential tested at 0.5mg/mL concentration exhibited reducing power activity with a maximum of 90% inhibition. The anticancer property by MTT assay on HeLa and HepG2 cells showed cytotoxic effect with IC50 of 50μg/mL each. The DNA fragmentation pattern observed in both HeLa and HepG2 cell indicated laddering pattern at 40μg/mL concentration. GC-MS analysis revealed that the significant peak corresponding at m/z 149 (M(+)) was identified as phthalate derivatives. The extract was further separated by HPLC with their retention times (t r) at 6.294min. The above-obtained results were also supported by molecular docking studies which provide an insight into ligand binding to the active site of the receptor. The in silico docking studies revealed better binding affinity with a binding energy of -5.87kJmol(-1) of the ligand toward topoisomerase II α.

hero.3453729

Jia, LL; Lou, XY; Guo, Y; Leung, KS; Zeng, EY. (2017). Occurrence of phthalate esters in over-the-counter medicines from China and its implications for human exposure. Environ Int 98: 137-142. http://dx.doi.org/10.1016/j.envint.2016.10.025.

Food, air, personal care products and indoor dust have been recognized as the main routes of exposure to phthalates in Chinese population, but other sources may have been overlooked, e.g., medicines. To fill the knowledge gap, phthalate esters were measured in 96 over-the-counter medicines made in China, including selected 71 Chinese patented medicines and 25 western medicines. It was found that none of the medicines was free of phthalates. The mean concentrations of individual phthalates ranged from 0.001μg/g (dicyclohexyl phthalate) to 5.85μg/g (diethyl phthalate). Among 9 targeted phthalates, di-n-butyl phthalate was the dominant congener, accounting for >65% of the total phthalates in all medicine samples, followed by di-(2-ethylhexyl) phthalate and diethyl phthalate. Phthalates in medicines appeared to derive from gastroresistant film coatings, plastic packing materials or phthalate contaminated rural herbal plants (especially for Chinese patented medicines). Daily human exposure to phthalates was estimated for local patients for one treatment cycle (e.g., one week) based on suggested consumption dosage and phthalate concentrations. Almost all exposure levels were below the guidelines suggested by the United States Environmental Protection Agency or European Food Safety Authority, indicating low health risk with

phthalates from consumption of the medicines. In addition, concentration levels of phthalates in patients would increase upon administration but are expected to decrease to the same values as those in patients before they took medicines in several days. Because the number of medicine samples was limited and the concentrations of phthalates varied in a large range, further investigations are needed to acquire more data for better assessment of human health effects for Chinese population. Capsule: Distribution of phthalate esters in over-the-counter medicines and related exposure for Chinese population are examined.

hero.3469545

Jo, A; Kim, H; Chung, H; Chang, N. (2016). Associations between Dietary Intake and Urinary Bisphenol A and Phthalates Levels in Korean Women of Reproductive Age. Int J Environ Res Public Health 13. http://dx.doi.org/10.3390/ijerph13070680.

Human exposure to Bisphenol A (BPA) and phthalates is a growing concern due to their association with harmful effects on human health, including a variety of disorders of the female reproductive system. The objective of this study was to investigate the association between food intake and urinary BPA and phthalates in Korean women of reproductive age. A cross-sectional study was conducted with 305 reproductive aged (30-49 years) females in Korea. Dietary intake was assessed using 24 h dietary recall, and urinary BPA and particular phthalates were measured using high performance liquid chromatography tandem mass spectrometry. After adjusting for covariates, beverage intake was positively associated with urinary BPA, and egg and egg product intake was negatively associated with urinary mono-n-butyl phthalate (MnBP) as well as mono (2-ethyl-5-oxohexyl) phthalate (MEOHP). Odds ratio for high BPA level (90th percentile) in women with >100 g of beverage consumption was significantly higher than for those who consumed 100 g. These results suggest that, in Korean women of reproductive age, some foods such as beverages and egg may be associated with body burdens of BPA, MnBP, MEHHP and MEOHP.

hero.3052885

Johns, LE; Cooper, GS; Galizia, A; Meeker, JD. (2015). Exposure assessment issues in epidemiology studies of phthalates [Review]. Environ Int 85: 27-39. http://dx.doi.org/10.1016/j.envint.2015.08.005.

PURPOSE: The purpose of this paper is to review exposure assessment issues that need to be addressed in designing and interpreting epidemiology studies of phthalates, a class of chemicals commonly used in consumer and personal care products. Specific issues include population trends in exposure, temporal reliability of a urinary metabolite measurement, and how well a single urine sample may represent longer-term exposure. The focus of this review is on seven specific phthalates: diethyl phthalate (DEP); di-n-butyl phthalate (DBP); diisobutyl phthalate (DiBP); butyl benzyl phthalate (BBzP); di(2-ethylhexyl) phthalate (DEHP); diisononyl phthalate (DiNP); and diisodecyl phthalate (DiDP).

METHODS: Comprehensive literature search using multiple search strategies.

RESULTS: Since 2001, declines in population exposure to DEP, BBzP, DBP, and DEHP have been reported in the United States and Germany, but DEHP exposure has increased in China. Although the half-lives of various phthalate metabolites are relatively short (3 to 18h), the intraclass correlation coefficients (ICCs) for phthalate metabolites, based on spot and first morning urine samples collected over a week to several months, range from weak to moderate, with a tendency toward higher ICCs (greater temporal stability) for metabolites of the shorter-chained (DEP, DBP, DiBP and BBzP, ICCs generally 0.3 to 0.6) compared with those of the longer-chained (DEHP, DiNP, DiDP, ICCs generally 0.1 to 0.3) phthalates. Additional research on optimal approaches to addressing the issue of urine dilution in studies of associations between biomarkers and different type of health effects is needed.

CONCLUSIONS: In conclusion, the measurement of urinary metabolite concentrations in urine could serve as a valuable approach to estimating exposure to phthalates in environmental epidemiology studies. Careful consideration of the strengths and limitations of this approach when interpreting study results is required.

hero.3469263

Johns, LE; Ferguson, KK; Meeker, JD. (2016). Relationships Between Urinary Phthalate Metabolite and Bisphenol A Concentrations and Vitamin D Levels in U.S. Adults: National Health and Nutrition Examination Survey (NHANES), 2005-2010. J Clin Endocrinol Metab 101: 4062-4069. http://dx.doi.org/10.1210/jc.2016-2134.

CONTEXT: Recent research suggests that environmental exposure to endocrine-

disrupting chemicals may alter circulating 25-hydroxyvitamin D [25(OH)D] levels in humans. To date, no studies have assessed the associations between phthalates and bisphenol A (BPA) and total 25(OH)D in the U.S. general population.

OBJECTIVE: To explore relationships between urinary concentrations of 11 phthalate metabolites and BPA and serum total 25(OH)D in a representative sample of U.S. adults.

DESIGN: A cross-sectional study.

SETTING: U.S. National Health and Nutrition Examination Survey, 2005-2010.

PATIENTS OR OTHER PARTICIPANTS: U.S. general adult population (aged 20 years).

INTERVENTIONS: None Main Outcome Measures: Serum total 25(OH)D measured by liquid chromatography-tandem mass spectrometry.

RESULTS: Metabolites of di(2-ethylhexyl) phthalate (DEHP) were consistently inversely associated with total 25(OH)D in the overall study population and in gender-stratified models. In the overall population, we detected a significant inverse relationship for the molar sum of DEHP metabolites (ΣDEHP), where an interquartile range increase in ΣDEHP was associated with a 1.90% decrease (95% confidence interval [CI], -3.64, -0.17) in total 25(OH)D. A positive association was detected for monoethyl phthalate. For BPA, we found a statistically significant inverse relationship in women, but not in men. In women, an interquartile range increase in urinary BPA was associated with a 3.71% decrease (95% CI, -6.41, -1.02) in total 25(OH)D.

CONCLUSIONS: Overall, our results provide suggestive evidence that environmental exposure to phthalates and BPA may alter circulating levels of total 25(OH)D in adults. Future human and animal studies are required to resolve the direction, temporality, and impact of these relationships.

hero.3052884

Kang, L; Wang, QM; He, QS; He, W; Liu, WX; Kong, XZ; Yang, B; Yang, C; Jiang, YJ; Xu, FL. (2016). Current status and historical variations of phthalate ester (PAE) contamination in the sediments from a large Chinese lake (Lake Chaohu). Environ Sci Pollut Res 23: 10393-10405. http://dx.doi.org/10.1007/s11356-015-5173-4.
The residual levels of phthalate esters (PAEs) in the surface and two core sediments from Lake Chaohu were measured with a gas chromatograph-mass spectrometer (GC-MS). The temporal-spatial distributions, compositions of PAEs, and their effecting factors were investigated. The results indicated that di-n-butyl phthalate (DnBP), diisobutyl phthalate (DIBP), and di(2-ethylhexyl) phthalate (DEHP) were three dominant PAE components in both the surface and core sediments. The residual level of total detected PAEs (PAEs) in the surface sediments (2.146 2.255μg/g dw) was lower than that in the western core sediments (10.615 9.733μg/g) and in the eastern core sediments (5.109 4.741μg/g). The average content of PAEs in the surface sediments from the inflow rivers (4.128 1.738μg/g dw) was an order of magnitude higher than those from the lake (0.323 0.093μg/g dw), and there were similar PAE compositions between the lake and inflow rivers. This finding means that there were important effects of PAE input from the inflow rivers on the compositions and distributions of PAEs in the surface sediments. An increasing trend was found for the residual levels of ΣPAEs, DnBP, and DIBP from the bottom to the surface in both the western and eastern core sediments. Increasing PAE usage with the population growth, urbanization, and industrial and agricultural development in Lake Chaohu watershed would result in the increasing production of PAEs and their resulting presence in the sediments. The significant positive relationships were also found between the PAE contents and the percentage of sand particles, as well as TOC contents in the sediment cores.

hero.3469559

Kariyazono, Y; Taura, J; Hattori, Y; Ishii, Y; Narimatsu, S; Fujimura, M; Takeda, T; Yamada, H. (2015). Effect of in utero exposure to endocrine disruptors on fetal steroidogenesis governed by the pituitary-gonad axis: a study in rats using different ways of administration. J Toxicol Sci 40: 909-916. http://dx.doi.org/10.2131/jts.40.909.
The effects of endocrine disruptors on testicular steroidogenesis in fetal rats were investigated in a study involving in utero exposure. In the major part of this study, pregnant rats at gestational day (GD)15 were given a single oral administration of the test substance, and then the expression of the following mRNAs in GD20 fetuses was determined: testicular steroidogenic acute-regulatory protein (StAR), a cholesterol transporter mediating the rate-limiting step of steroidogenesis, a ß-subunit of pituitary luteinizing hormone (LH), and a regulator of gonadal steroidogenesis. Among the substances tested, only di(2-ethylhexyl)phthalate (DEHP) reduced the expression of fetal testicular StAR. The others listed below exhibited little effect on fetal StAR: 2,2',4,4'-tetrabromodiphenylether, tributyltin chloride, atrazine, permethrin,

cadmium chloride (Cd), lead acetate (Pb) and methylmercury (CH3HgOH). None of them, including DEHP, lacked the ability to reduce the expression of pituitary LHß mRNA. The present study also examined the potential of metals as modifiers of fetal steroidogenesis by giving them to pregnant dams in drinking water during GD1 and GD20. Under these conditions, Cd and Pb at a low concentration (0.01 ppm) significantly attenuated the fetal testicular expression of StAR mRNA without a concomitant reduction in LHß. No such effect was detected with CH3HgOH even at 1 ppm. These results suggest that: 1) DEHP, Cd and Pb attenuate the fetal production of sex steroids by directly acting on the testis, and 2) chronic treatment during the entire gestational period is more useful than a single administration for determining the hazardous effect of a suspected endocrine disruptor on fetal steroidogenesis.

hero.3469376

Katsikantami, I; Sifakis, S; Tzatzarakis, MN; Vakonaki, E; Kalantzi, OI; Tsatsakis, AM; Rizos, AK. (2016). A global assessment of phthalates burden and related links to health effects [Review]. Environ Int 97: 212-236. http://dx.doi.org/10.1016/j.envint.2016.09.013.

Phthalates are ubiquitous environmental contaminants which are used in industry as plasticizers and additives in cosmetics. They are classified as Endocrine Disrupting Chemicals (EDCs) which impair the human endocrine system inducing fertility problems, respiratory diseases, childhood obesity and neuropsychological disorders. The aim of this review is to summarize the current state of knowledge on the toxicity that phthalates pose in humans based on human biomonitoring studies conducted over the last decade. Except for conventional biological matrices (such as urine and serum), amniotic fluid, human milk, semen, saliva, sweat, meconium and human hair are also employed for the estimation of exposure and distribution of pollutants in the human body, although data are not enough yet. Children are highly exposed to phthalates relative to adults and in most studies children's daily intake surpasses the maximum reference dose (RfD) set from US Environmental Protection Agency (US EPA). However, the global trend is that human exposure to phthalates is decreasing annually as a result of the strict regulations applied to phthalates.

hero.3479548

Kim, B; Kwon, B; Jang, S; Kim, PG; Ji, K. (2016). Major benzophenone concentrations and influence of food consumption among the general population in Korea, and the association with oxidative stress biomarker. Sci Total Environ 565: 649-655. http://dx.doi.org/10.1016/j.scitotenv.2016.05.009.

Benzophenones (BPs) have been used as sunscreen agents and as ultraviolet stabilizers in plastic surface coatings for food packaging. However, few studies have been performed to examine the level of human exposure to BPs and the potential sources of such exposure. We evaluated the exposure levels to six major BPs (BP-1, BP-2, BP-3, BP-4, BP-8, and 4-hydroxybenzophenone (4-OH-BP)) among the adult population in two cities in Korea, and investigated the potential dietary sources of the BPs. Urinary levels of malondialdehyde (MDA) as an oxidative stress biomarker as well as their association with the levels of BPs were also analyzed. Among the six BPs analyzed, 4-OH-BP, BP-1, BP-3, and BP-4 were detected in 77%, 49%, 27%, and 21% of the population, respectively. BP concentrations were relatively higher in younger (people in their 20s and 30s) cosmetic users and leaner women. Even after the adjustment of age, body mass index, and cosmetic use, the consumption of frozen storage food, instant noodles, and instant coffee was significantly correlated with urinary BPs, and these associations were sex-dependent. No significant correlation was observed between the levels of BPs and levels of MDA. The results of the present study will be useful for developing plans of public health management of BPs.

hero.3469444

Kim, KN; Lee, MR; Choi, YH; Hwang, H; Oh, SY; Park, C; Hong, YC. (2016). Association between phthalate exposure and lower handgrip strength in an elderly population: a repeated-measures study. Environ Health 15: 93. http://dx.doi.org/10.1186/s12940-016-0176-2.

BACKGROUND: Decreased muscle strength can lead to adverse health outcomes in the elderly. A potential association between phthalate exposure and muscle strength was suggested previously, but has not been investigated directly. We hypothesized that phthalate exposure is associated with lower handgrip strength and that the association is modified by the dietary omega-6 to omega-3 ratio.

METHODS: We analyzed 1,228 participants (60years of age) recruited in Seoul and Asan, Republic of Korea. The study participants were surveyed up to three times between 2012 and 2015. At

every survey, we collected urine samples and measured handgrip strength twice for each hand. The associations between urine phthalate metabolite concentrations and handgrip strength were evaluated using linear mixed models. Based on dietary information from 391 individuals who participated in the first survey in Seoul, we evaluated the heterogeneity of the association for those with high and low omega-6 to omega-3 ratios, using 8.81 (the 75th quantile) as a cutoff value.

RESULTS: Log-transformed creatinine-adjusted concentrations of mono-(2-ethyl-5-oxohexyl phthalate (MEOHP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), and mono-n-butyl phthalate (MnBP) were inversely associated with all measured handgrip strengths (β = -0.69 to -0.42, all p-values < 0.05). Associations between phthalate biomarkers and handgrip strength did not differ by sex. When the dietary subgroup was stratified by the omega-6 to omega-3 ratio, the associations were stronger among participants with high ratios.

CONCLUSIONS: We found inverse associations between phthalate biomarkers and handgrip strength in the elderly; this association was modified by the dietary omega-6 to omega-3 ratio.

hero.3466584

Kim, YA; Kho, Y; Chun, KC; Koh, JW; Park, JW; Bunderson-Schelvan, M; Cho, YH. (2016). Increased Urinary Phthalate Levels in Women with Uterine Leiomyoma: A Case-Control Study. Int J Environ Res Public Health 13. http://dx.doi.org/10.3390/ijerph13121247.

We assessed the urinary concentration of 16 phthalate metabolites in 57 women with and without uterine leiomyoma (n = 30 and 27; respectively) to determine the association between phthalate exposure and uterine leiomyoma. To evaluate exposure to di-(2-ethylhexyl) phthalate (DEHP); we calculated the molar sum of DEHP metabolites; 3-DEHP (combining mono-(2-ethylhexyl) phthalate (MEHP); mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP); and mono-(2-ethyl-5-oxohexyl) phthalate); 4-DEHP (3-DEHP plus mono-(2-ethyl-5-carboxypentyl) phthalate); and 5-DEHP (4-DEHP plus mono (2-(carboxylmethyl)hexyl) phthalate (2cx-MMHP)). The log transformed urinary levels of MEHP; MEHHP; 2cx-MMHP; 3-DEHP; 4-DEHP; and 5-DEHP in the leiomyoma group were significantly higher than those of controls. When we adjusted for age; waist circumference; and parity using multiple logistic regression analyses; we found log 3-DEHP (OR = 10.82; 95% CI = 1.25; 93.46) and 4-DEHP (OR = 8.78; 95% CI = 1.03; 75.29) were significantly associated with uterine leiomyoma. Our findings suggest an association between phthalate exposure and uterine leiomyoma. However; larger studies are needed to investigate potential interactions between phthalate exposure and uterine leiomyoma.

hero.3469204

Koch, HM; Rüther, M; Schütze, A; Conrad, A; Pälmke, C; Apel, P; Brüning, T; Kolossa-Gehring, M. (2016). Phthalate metabolites in 24-h urine samples of the German Environmental Specimen Bank (ESB) from 1988 to 2015 and a comparison with US NHANES data from 1999 to 2012. Int J Hyg Environ Health. http://dx.doi.org/10.1016/j.ijheh.2016.11.003.

The German Environmental Specimen Bank (ESB) continuously collects 24-h urine samples since the early 1980s in Germany. In this study we analyzed 300 urine samples from the years 2007 to 2015 for 21 phthalate metabolites (representing exposure to 11 parent phthalates) and combined the data with two previous retrospective measurement campaigns (1988 to 2003 and 2002 to 2008). The combined dataset comprised 1162 24-h urine samples spanning the years 1988 to 2015. With this detailed set of human biomonitoring data we describe the time course of phthalate exposure in Germany over a time frame of 27 years. For the metabolites of the endocrine disrupting phthalates di(2-ethylhexyl) phthalate (DEHP), di-n-butyl phthalate (DnBP) and butylbenzyl phthalate (BBzP) we observed a roughly ten-fold decline in median metabolite levels from their peak levels in the late 1980s/early 1990s compared to most recent levels from 2015. Probably, bans (first enacted in 1999) and classifications/labelings (enacted in 2001 and 2004) in the European Union lead to this drop. A decline in di-isobutyl phthalate (DiBP) metabolite levels set in only quite recently, possibly due to its later classification as a reproductive toxicant in the EU in 2009. In a considerable number of samples collected before 2002 health based guidance values (BE, HBM I) have been exceeded for DnBP (27.2%) and DEHP (2.3%) but also in recent samples some individual exceedances can still be observed (DEHP 1.0%). A decrease in concentration for all low molecular weight phthalates, labelled or not, was seen in the most recent years of sampling. For the high molecular weight phthalates, DEHP seems to have been substituted in part by di-isononyl phthalate (DiNP), but DiNP metabolite levels have also been declining in the last years. Probably, non-phthalate alternatives increasingly take over for the phthalates in Germany. A

comparison with NHANES (National Health and Nutrition Examination Survey) data from the United States covering the years 1999 to 2012 revealed both similarities and differences in phthalate exposure between Germany and the US. Exposure to critical phthalates has decreased in both countries with metabolite levels more and more aligning with each other, but high molecular weight phthalates substituting DEHP (such as DiNP) seem to become more important in the US than in Germany.

hero.3453174

Kong, L; Kadokami, K; Duong, HT; Chau, HT. (2016). Screening of 1300 organic micro-pollutants in groundwater from Beijing and Tianjin, North China. Chemosphere 165: 221-230. http://dx.doi.org/10.1016/j.chemosphere.2016.08.084.
Groundwater contamination in China has become a growing public concern because of the country's rapid economic development and dramatically increasing fresh water demand. However, there is little information available on groundwater quality, particularly with respect to trace organic micro-pollutants contamination. This study was undertaken to investigate the occurrence of 1300 pollutants at 27 groundwater sites in Beijing and Tianjin, North China. Seventy-eight chemicals (6% of the targeted compounds) were detected in at least one sampling point; observed chemicals included polycyclic aromatic hydrocarbons (PAHs), pesticides, plasticizers, antioxidants, pharmaceuticals and other emerging compounds. Chemicals with a frequency of detection over 70% were 2-ethyl-1-hexanol (median concentration 152ngL(-1)), benzyl alcohol (582ngL(-1)), 2-phenoxy-ethanol (129ngL(-1)), acetophenone (74ngL(-1)), pentamethylbenzene (51ngL(-1)), nitrobenzene (40ngL(-1)) and dimethyl phthalate (64ngL(-1)). Pesticides with concentrations exceeding the EU maximum residual limits (MRL) of 0.1μgL(-1) were 1,4-dichlorobenzene, oxadixyl, diflubenzuron, carbendazim, diuron, and the E and Z isomers of dimethomorph. Naphthalene and its 7 alkylated derivatives were widely observed at maximum concentration up to 30μgL(-1), which, although high, is still below the Australian drinking water guidelines of 70μgL(-1). The risk assessment indicated there is no human health risk through the oral consumption from most wells, although there were four wells in which total seven compounds were found at the concentrations with a potential adverse health effects. This work provides a wide reconnaissance on broad spectrum of organic micro-contaminants in groundwater in North China.

hero.3469563

Konkel, L. (2015). Exploring a Little-Known Pathway: Dermal Exposure to Phthalates in Indoor Air [Comment]. Environ Health Perspect 123: A267. http://dx.doi.org/10.1289/ehp.123-A267.

hero.3366073

Kubwabo, C; Fan, X; Rasmussen, P, atE; Wu, F; Kosarac, I. (2016). Expanding the number of phthalates monitored in house dust. Int J Environ Anal Chem 96: 667-681. http://dx.doi.org/10.1080/03067319.2016.1180380.
Phthalates have been used as plasticisers for several decades in various industry and consumer products. A method was developed for the determination of 13 not commonly monitored phthalates in household dust. The method was based on solvent extraction using sonication, sample clean-up by solid phase extraction (SPE), and analysis using isotope dilution gas chromatography-tandem mass spectrometry (GC/MS/MS). The method was applied to the analysis of dust samples collected using two vacuum sampling techniques from 38 urban Canadian homes: a sample of fresh or active' dust (FD) collected by technicians and a composite sample taken from the household vacuum cleaner (HD). Spearman rank correlations between HD and FD samples were significant for six phthalates with median concentrations above their method detection limits (MDLs), suggesting that the HD samples provide comparable results with FD samples. Seven phthalates were detected and quantified in a Canada-wide set of 126 household dust samples, among which six phthalates were detected at frequencies higher than 87%, with median (range) concentrations of 1.9 (<0.42-240) (g/g) for diisohexyl phthalate (DIHxP), 3.8 (<0.16-260) (g/g) for di-n-heptyl phthalate (DHepP), 6.6 (<1.1-1170) (g/g) for diisooctyl phthalate (DIOP), 1.1 (<0.12-390) (g/g) for di-n-octyl phthalate (DOP), 6.3 (<0.16-430) (g/g) for dinonyl phthalate (DNP), and 1.8 (<0.18-850) (g/g) for di-n-decyl phthalate (DDP). High detection frequencies and widely scattered concentration levels of these phthalates in this preliminary set of 126 samples suggested a high variability in potential exposure to phthalates in Canadian homes. NIST SRM 2585 (organic contaminants in house dust) was also analysed; eight phthalates were detected, with concentrations ranging from 6.0g/g for DOP to 79g/g for DIHxP. The results from SRM 2585 may contribute to the certification of phthalate concentration values in this SRM.

hero.3479537

Kumar, S; Kumar, A; Kumar, N; Roy, P; Sondhi, SM. (2016). Grinding and Microwave-assisted Synthesis of Heterocyclic Molecules in High Yields and Their Biological Evaluation. J Heterocycl Chem 53: 1761-1770. http://dx.doi.org/10.1002/jhet.2481.

Cis-cyclohexane1,2-dicarboxylic acid (1a), phthalic acid (1b), and pyrazine 2,3-dicarboxylic acid (1c) on grinding with hydrazine hydrate (2a) gave 2-aminohexahydro-1H-isoindole-1,3(2H)-dione (3a), 2-amino1H-isoindole-1,3(2H)-dione (3b), and 6-amino-5H-pyrrolo[3,4-b]pyrazine-5,7(6H)-dione (3c), respectively. Condensation of (3a-c) with aldehydes (4x-z) and 2-cyanopyridine, 4-cyanopyridine, 2-cyanopyrazine (5x-z) under microwave irradiation gave corresponding azomethine (6ax-cz) and amidine (7ax-cz) derivatives, respectively. Fully characterized azomethine (6ax-cz) and amidine (7ax-cz) derivatives were screened for anti-inflammatory and anticancer activity against five human cancer cell lines. Compound 7cx exhibited 35% anti-inflammatory activity at a dose of 50 mg/kg p.o. whereas standard drug ibuprofen showed 39% activity at a dose of 50 mg/kg p.o. Compounds 6bz, 7cx, 7cz (breast T47D), 6bz, 6cy (lung NCI H-522), 6bx, 7bz (colon HCT-15), 6bz (ovary PA-1) and 6bx, and 6cz (liver HepG-2) exhibited good (35-41% inhibition at 10 mu M c) anticancer activity. IC50 values of 6bx, 6bz, 6cy, 6cz, 7bz, 7cx, and 7cz against various cancer cell lines and normal cell (COS-1) are also reported.

hero.3456656

Kumari, M; Ghosh, P; Thakur, IS. (2016). Landfill leachate treatment using bacto-algal co-culture: An integrated approach using chemical analyses and toxicological assessment. Ecotoxicol Environ Saf 128: 44-51. http://dx.doi.org/10.1016/j.ecoenv.2016.02.009.

The present study aims to evaluate the feasibility of leachate treatment using a synergistic approach by microalgae and bacteria. Leachate from one of the landfill of Northern India showed the presence of various toxic organic contaminants like naphthalene, benzene, phenol and their derivatives, napthols, pesticides, epoxides, phthalates and halogenated organic compounds. ICP-AES analysis revealed high concentrations of Zn, Cr, Fe, Ni, and Pb beyond the maximum permissible limit of discharge. Bacto-algal co-culture was found to be the most efficient in removal of toxic organic contaminants and heavy metals. Further, detoxification efficiency of bacto-algal treatment was evaluated by Methyl tetrazolium (MTT) assay for cytotoxicity and alkaline comet assay for genotoxicity using hepatoma HepG2 cells. Reduction in toxicity was confirmed by an increase in LC50 by 1.9 fold and reduction in Olive Tail Moment by 40.6 fold after 10 days of treatment. Results of the study indicate bioremediation and detoxification potency of bacto-algal co-culture for leachate treatment.

hero.3479553

Kushwaha, M; Verma, S; Chatterjee, S. (2016). Profenofos, an Acetylcholinesterase-Inhibiting Organophosphorus Pesticide: A Short Review of Its Usage, Toxicity, and Biodegradation. J Environ Qual 45: 1478-1489. http://dx.doi.org/10.2134/jeq2016.03.0100.

Pesticides play an important role in the protection of different crops. Among the diverse sets of pesticides used all over the world, the organophosphates are the most widely used group. Profenofos [O-(4-bromo-2-chlorophenyl) O-ethyl S-propyl phosphorothioate] is one of the most largely used organophosphate insecticides on field crops, vegetables, and fruit crops. The World Health Organization classifies this compound as moderately hazardous (Toxicity Class II), and its residues have been found in vegetables like okra [(L.) Moench], gooseberries (sp.), green chilies [(L.)], curry leaves [(L.) Spreng], mint leaves [(L.)], and coriander leaves [(L.)]. Dietary intake of profenofos (PFF) is the major exposure pathway for humans. When applied to agricultural fields, PFF residues spread into every part of the environment: ambient air, surface water, and soil. In this review, we discuss the worldwide usage of PFF pesticide, its toxic effects on humans and other living organisms in the environment, and biodegradation of this chemical by various microbial strains. To date, no complete biodegradation pathway has been established for PFF pesticide, calling for a study of this nature.

hero.3479546

Landrigan, PJ; Sly, JL; Ruchirawat, M; Silva, ER; Huo, X; Diaz-Barriga, F; Zar, HJ; King, M; Ha, EH; Asante, KA; Ahanchian, H; Sly, PD. (2016). Health Consequences of Environmental Exposures: Changing Global Patterns of Exposure

and Disease [Review]. 82: 10-19. http://dx.doi.org/10.1016/j.aogh.2016.01.005.
Environmental pollution is a major cause of disease and death. Exposures in early life are especially dangerous. Patterns of exposure vary greatly across countries. In low-income and lower middle income countries (LMICs), infectious, maternal, neonatal, and nutritional diseases are still major contributors to disease burden. By contrast, in upper middle income and high-income countries noncommunicable diseases predominate. To examine patterns of environmental exposure and disease and to relate these patterns to levels of income and development, we obtained publically available data in 12 countries at different levels of development through a global network of World Health Organization Collaborating Centres in Children's Environmental Health. Pollution exposures in early life contribute to both patterns. Chemical and pesticide pollution are increasing, especially in LMICs. Hazardous wastes, including electronic waste, are accumulating. Pollution-related chronic diseases are becoming epidemic. Future Global Burden of Disease estimates must pay increased attention to the short- and long-term consequences of environmental pollution.

hero.3208507

Lassen, TH; Frederiksen, H; Kyhl, HB; Swan, SH; Main, KM; Andersson, AM; Lind, DV; Husby, S; Wohlfahrt-Veje, C; Skakkebæk, NE; Jensen, TK. (2016). Prenatal Triclosan Exposure and Anthropometric Measures including Anogenital Distance in Danish Infants. Environ Health Perspect 124: 1261-1268. http://dx.doi.org/10.1289/ehp.1409637.
BACKGROUND: Triclosan (TCS) is widely used as an antibacterial agent in consumer products such as hand soap and toothpaste and human exposure is widespread. TCS is suspected of having endocrine disrupting properties, but few human studies have examined the developmental effects of prenatal TCS exposure.

OBJECTIVES: To prospectively examine associations between prenatal TCS exposure and anthropometric measures at birth and anogenital distance (AGD) at three months of age.

METHODS: Pregnant women from the Odense Child Cohort (n=514) provided urine samples around gestational week 28 (median 28.7 weeks, range 26.4 - 34.0) and urinary TCS concentration was measured by LC-MS/MS. Multiple linear regression analysis was used to examine associations between prenatal TCS exposure and measures of size at birth (birth weight, length, head and abdominal circumference) and AGD at three months of age (median 3.3 months, range 2.3 to 6.7 months) controlling for potential confounders.

RESULTS: Newborn boys in the highest quartile of prenatal TCS exposure had a 0.7 cm (95% CI: -1.2, -0.1, p=0.01) smaller head circumference compared with boys in the lowest quartile. Additionally in boys, inverse associations of borderline statistical significance between prenatal TCS exposure and abdominal circumference at birth and AGD at three months were observed (p-values <0.10). Prenatal TCS exposure was not significantly associated with any of the outcomes in girls. However, fewer girls had AGD measured and we observed no significant interactions between child sex and prenatal TCS-exposure in anthropometric measures at birth.

CONCLUSION: Prenatal TCS-exposure was associated with reduced head and abdominal circumference at birth and reduced AGD at three months of age in boys, although the two latter findings were statistically non-significant. These findings require replication, but are compatible with an anti-androgenic effect of prenatal TCS exposure on fetal growth in boys.

hero.3469275

Latini, G; Dipaola, L; Andreassi, MG; Rocchiccioli, S; Massaro, M; Picano, E. (2016). Interaction between Ionizing Radiation and Phthalates: An Unrecognized Risk for Human Health? Mini Rev Med Chem.
Ionizing radiation has been shown to impact and possibly alter the normal structure and function of living cells and is dangerous for human health, especially when exposure occurs early in life. Additionally, radiation can interact with other dangerous substances in the same environment, such as phthalates. Phthalates are a group of multifunctional molecules used in a wide range of consumer products, as plasticizers to impart flexibility, durability and strength to otherwise rigid polyvinyl chloride. They are not chemically bound to polyvinyl chloride, and thus migrate into the environment with time and use, becoming ubiquitous environmental contaminants. There is growing concern about the effect that exposure to ionizing radiation and phthalates can have on human health, and the biological effects of this cumulative exposure are particularly troubling in infants due to children's inherent sensitivity. Pediatric patients are exposed to numerous plastic medical devices and often require multiple radiologic examinations for their complex medical conditions. Risk assessment requires a more complete evaluation of the effects of simultaneous and

cumulative exposure, especially in high-risk patients.

hero.3469470

Laurenzana, EM; Coslo, DM; Vigilar, MV; Roman, AM; Omiecinski, CJ. (2016). Activation of the Constitutive Androstane Receptor by Monophthalates. Chem Res Toxicol 29: 1651-1661. http://dx.doi.org/10.1021/acs.chemrestox.6b00186.

Humans in industrialized areas are continuously exposed to phthalate plasticizers, prompting concerns of their potential toxicities. Previous studies from our laboratory and others have shown that various phthalates activate several mammalian nuclear receptors, in particular the constitutive androstane receptor (CAR), the pregnane X receptor (PXR), and the peroxisomal proliferator-activated receptors (PPARs), although often at concentration levels of questionable relevance to human exposure. We discovered that di(2-ethylhexyl) phthalate (DEHP) and di-isononyl phthalate (DiNP), two of the highest volume production agents, were potent activators of human CAR2 (hCAR2), a unique human CAR splice variant and, to a lesser degree, human PXR (hPXR). These diphthalates undergo rapid metabolism in mammalian systems, initially to their major monophthalate derivatives MEHP and MiNP. Although MEHP and MiNP are reported activators of the rodent PPARs, with lower affinities for the corresponding human PPARs, it remains unclear whether these monophthalate metabolites activate hCAR2 or hPXR. In this investigation, we assessed the relative activation potential of selected monophthalates and other low molecular weight phthalates against hCAR, the most prominent hCAR splice variants, as well as hPXR and human PPAR. Using transactivation and mammalian two-hybrid protein interaction assays, we demonstrate that these substances indeed activate hCARs and hPXR but to varying degrees. MEHP and MiNP exhibit potent activation of hCAR2 and hPXR with higher affinities for these receptors than for the hPPARs. The rank order potency for MEHP and MiNP was hCAR2 > hPXR > hPPARs. Results from primary hepatocyte experiments also reflect the MEHP and MiNP upregulation of the respective human target genes. We conclude that both di- and monophthalates are potently selective hCAR2 activators and effective hPXR activators. These results implicate these targets as important mediators of selective phthalate effects in humans. The striking differential affinities for these compounds between human and rodent nuclear receptors further implies that biological results obtained from rodent models may be of only limited relevance for interpolating phthalate-mediated effects in humans.

hero.3469483

Lea, RG; Byers, AS; Sumner, RN; Rhind, SM; Zhang, Z; Freeman, SL; Moxon, R; Richardson, HM; Green, M; Craigon, J; England, GC. (2016). Environmental chemicals impact dog semen quality in vitro and may be associated with a temporal decline in sperm motility and increased cryptorchidism. Sci Rep 6: 31281. http://dx.doi.org/10.1038/srep31281.

Adverse temporal trends in human semen quality and cryptorchidism in infants have been associated with exposure to environmental chemicals (ECs) during development. Here we report that a population of breeding dogs exhibit a 26 year (1988-2014) decline in sperm quality and a concurrent increased incidence of cryptorchidism in male offspring (1995-2014). A decline in the number of males born relative to the number of females was also observed. ECs, including diethylhexyl phthalate (DEHP) and polychlorinated bisphenol 153 (PCB153), were detected in adult dog testes and commercial dog foods at concentrations reported to perturb reproductive function in other species. Testicular concentrations of DEHP and PCB153 perturbed sperm viability, motility and DNA integrity in vitro but did not affect LH stimulated testosterone secretion from adult testis explants. The direct effects of chemicals on sperm may therefore contribute to the decline in canine semen quality that parallels that reported in the human.

hero.3479520

Lee, J; Lee, YA, h; Jung, H, aeW; Kim, H, waY; Lee, GM, in; Kim, S, oY; Jeong, KA; Choi, KH, ee; Lim, YH, ee; Bae, S; Hong, Y, unC; Shin, CH, o; Yang, S, eiWon. (2016). Exposure to Phthalates Is Associated with Overweight or Obesity in 4-Year-Old Children. Horm Res 86: 307-307.

hero.3466565

Lee, WC; Fisher, M; Davis, K; Arbuckle, TE; Sinha, SK. (2016). Identification of chemical mixtures to which Canadian pregnant women are exposed: The MIREC Study. Environ Int. http://dx.doi.org/10.1016/j.envint.2016.12.015.

Depending on the chemical and the outcome, prenatal exposures to environmental chemicals can lead to adverse effects on the pregnancy and child development, especially if exposure occurs during early gestation. Instead of focusing on prenatal exposure to individual chemicals, more studies have taken into account that humans are exposed to multiple environmental chemicals on a daily basis. The objectives of this analysis were to identify the pattern of chemical mixtures to which women are exposed and to characterize women with elevated exposures to various mixtures. Statistical techniques were applied to 28 chemicals measured simultaneously in the first trimester and socio-demographic factors of 1744 participants from the Maternal-Infant Research on Environment Chemicals (MIREC) Study. Cluster analysis was implemented to categorize participants based on their socio-demographic characteristics, while principal component analysis (PCA) was used to extract the chemicals with similar patterns and to reduce the dimension of the dataset. Next, hypothesis testing determined if the mean converted concentrations of chemical substances differed significantly among women with different socio-demographic backgrounds as well as among clusters. Cluster analysis identified six main socio-demographic clusters. Eleven components, which explained approximately 70% of the variance in the data, were retained in the PCA. Persistent organic pollutants (PCB118, PCB138, PCB153, PCB180, OXYCHLOR and TRANSNONA) and phthalates (MEOHP, MEHHP and MEHP) dominated the first and second components, respectively, and the first two components explained 25.8% of the source variation. Prenatal exposure to persistent organic pollutants (first component) were positively associated with women who have lower education or higher income, were born in Canada, have BMI 25, or were expecting their first child in our study population. MEOHP, MEHHP and MEHP, dominating the second component, were detected in at least 98% of 1744 participants in our cohort study; however, no particular group of pregnant women was identified to be highly exposed to phthalates. While widely recognized as important to studying potential health effects, identifying the mixture of chemicals to which various segments of the population are exposed has been problematic. We present an approach using factor analysis through principal component method and cluster analysis as an attempt to determine the pregnancy exposome. Future studies should focus on how to include these matrices in examining the health effects of prenatal exposure to chemical mixtures in pregnant women and their children.

hero.3469374

Leng, G; Gries, W. (2016). New specific and sensitive biomonitoring methods for chemicals of emerging health relevance [Review]. Int J Hyg Environ Health. http://dx.doi.org/10.1016/j.ijheh.2016.09.014.

In this publication the challenges to cope for the aim to obtain innovative biomonitoring methods in our laboratory are visualized for di(2-propylheptyl)phthalate, 2-mercaptobenzothiazole, 3,5-di-tert-butyl-4-hydroxytoluene, 4-nonylphenol, 4-tert-octylphenol, 3-(4-methylbenzylidene)camphor, 4,4'-methylene diphenyl diisocyanate, and Hexabromocyclododecane. For these substances new specific markers were explored based on animal or human kinetic data with urine being the preferred matrix compared to blood. The determination of these markers was complex in all cases, because the sample preparation as well as the detection by high performance liquid chromatography, capillary gas chromatography coupled to tandem mass spectrometers or high resolution mass spectrometry should enable the lowest possible detection limit by use of minimal biological sample volumes. To get a first hint of a possible background level, the analytical methods were applied to urine samples of about 40 persons for each chemical. For Di(2-propylheptyl)phthalate and 2-Mercaptobenzothiazole first results are presented from population biomonitoring.

hero.3350198

Lenoir, A; Boulay, R; Dejean, A; Touchard, A; Cuvillier-Hot, V. (2016). Phthalate pollution in an Amazonian rainforest. Environ Sci Pollut Res 23: 16865-16872. http://dx.doi.org/10.1007/s11356-016-7141-z.

Phthalates are ubiquitous contaminants and endocrine-disrupting chemicals that can become trapped in the cuticles of insects, including ants which were recognized as good bioindicators for such pollution. Because phthalates have been noted in developed countries and because they also have been found in the Arctic, a region isolated from direct anthropogenic influence, we hypothesized that they are widespread. So, we looked for their presence on the cuticle of ants gathered from isolated areas of the Amazonian rainforest and along an anthropogenic gradient of pollution (rainforest vs. road sides vs. cities in French Guiana). Phthalate pollution (mainly di(2-ethylhexyl) phthalate (DEHP)) was higher on ants gathered in cities and along road sides than on those collected in the pristine rainforest, indicating that it follows a human-

mediated gradient of disturbance related to the use of plastics and many other products that contain phthalates in urban zones. Their presence varied with the ant species; the cuticle of Solenopsis saevissima traps higher amount of phthalates than that of compared species. However, the presence of phthalates in isolated areas of pristine rainforests suggests that they are associated both with atmospheric particles and in gaseous form and are transported over long distances by wind, resulting in a worldwide diffusion. These findings suggest that there is no such thing as a "pristine" zone.

hero.3070962

Leuenberger, N; Barras, L; Nicoli, R; Robinson, N; Baume, N; Lion, N; Barelli, S; Tissot, JD; Saugy, M. (2015). Urinary di-(2-ethylhexyl) phthalate metabolites for detecting transfusion of autologous blood stored in plasticizer-free bags. Transfusion 56: 571-578. http://dx.doi.org/10.1111/trf.13408.

BACKGROUND: Autologous blood transfusion (ABT) efficiently increases sport performance and is the most challenging doping method to detect. Current methods for detecting this practice center on the plasticizer di(2-ethlyhexyl) phthalate (DEHP), which enters the stored blood from blood bags. Quantification of this plasticizer and its metabolites in urine can detect the transfusion of autologous blood stored in these bags. However, DEHP-free blood bags are available on the market, including n-butyryl-tri-(n-hexyl)-citrate (BTHC) blood bags. Athletes may shift to using such bags to avoid the detection of urinary DEHP metabolites.

STUDY DESIGN AND METHODS: A clinical randomized double-blinded two-phase study was conducted of healthy male volunteers who underwent ABT using DEHP-containing or BTHC blood bags. All subjects received a saline injection for the control phase and a blood donation followed by ABT 36 days later. Kinetic excretion of five urinary DEHP metabolites was quantified with liquid chromatography coupled with tandem mass spectrometry.

RESULTS: Surprisingly, considerable levels of urinary DEHP metabolites were observed up to 1 day after blood transfusion with BTHC blood bags. The long-term metabolites mono-(2-ethyl-5-carboxypentyl) phthalate and mono-(2-carboxymethylhexyl) phthalate were the most sensitive biomarkers to detect ABT with BTHC blood bags. Levels of DEHP were high in BTHC bags (6.6%), the tubing in the transfusion kit (25.2%), and the white blood cell filter (22.3%).

CONCLUSIONS: The BTHC bag contained DEHP, despite being labeled DEHP-free. Urinary DEHP metabolite measurement is a cost-effective way to detect ABT in the antidoping field even when BTHC bags are used for blood storage.

hero.3102874

Leung, MC; Phuong, J; Baker, NC; Sipes, NS; Klinefelter, GR; Martin, MT; Mclaurin, KW; Setzer, RW; Darney, SP; Judson, RS; Knudsen, TB. (2015). Systems Toxicology of Male Reproductive Development: Profiling 774 Chemicals for Molecular Targets and Adverse Outcomes. Environ Health Perspect 0: 1-48. http://dx.doi.org/10.1289/ehp.1510385.

BACKGROUND: Trends in male reproductive health have been reported for increased rates of testicular germ cell tumors, low semen quality, cryptorchidism, and hypospadias, which have been associated with prenatal environmental chemical exposure based on human and animal studies.

OBJECTIVE: The present study aimed to identify significant correlations between environmental chemicals, molecular targets, and adverse outcomes across a broad chemical landscape with emphasis on developmental toxicity of the male reproductive system.

METHODS: We used U.S. EPA's animal study database (ToxRefDB) and a comprehensive literature analysis to identify 774 chemicals that have been evaluated for adverse effects on male reproductive parameters, and then used U.S. EPA's in vitro high-throughput screening (HTS) database (ToxCastDB) to profile their bioactivity across ~800 molecular and cellular features.

RESULTS: A phenotypic hierarchy of testicular atrophy, sperm effects, tumors, and malformations, a composite resembling the human Testicular Dysgenesis Syndrome (TDS) hypothesis, was observed in 281 chemicals. A subset of 54 chemicals with male developmental consequences had in vitro bioactivity on molecular targets that could be condensed into 156 gene annotations in a bipartite network.

CONCLUSION: Computational modeling of available in vivo and in vitro data for chemicals that produce adverse effects on male reproductive endpoints revealed a phenotypic hierarchy across animal studies consistent with the human TDS hypothesis. We confirmed the known role of estrogen and androgen signaling pathways in rodent TDS, and importantly, broadened the list of molecular targets to

include retinoic acid signaling, vascular remodeling proteins, G-protein coupled receptors (GPCRs), and cytochrome-P450s.

hero.3230087

Li, B, in; Xu, X; Zhu, Y; Cao, J; Zhang, Y; Huo, X, ia. (2016). Neonatal phthalate ester exposure induced placental MTs, FATP1 and HFABP mRNA expression in two districts of southeast China. Sci Rep 6: 21004. http://dx.doi.org/10.1038/srep21004.

Plastic production releases phthalate esters (PAEs), which can alter the expression of metallothioneins (MTs), fatty acid transport protein 1 (FATP1) and heart fatty acid binding protein (HFABP). A total of 187 mother-infant pairs were recruited, 127 from Chenghai (high exposed group) and 60 from Haojiang (low exposed group), to investigate the association between neonatal PAE exposure and mRNA expression of placental MTs, FATP1 and HFABP. Umbilical cord blood and placenta samples were collected for measuring five PAE concentrations and detecting mRNA levels of MTs, FATP1 and HFABP. Butylbenzyl phthalate (BBP), di(2-ethylhexyl) phthalate (DEHP), di-n-octyl phthalate (DNOP) were significantly higher in the high exposed group compared to the low exposed group. FATP1 and HFABP mRNA in the high exposed group were higher than that in the low exposed group while MT-1A was contrary. Both dimethyl phthalate (DMP) and DEHP were correlated with higher MT and MT-2A expression, while diethyl phthalate (DEP) was also positively correlated with MT-1A and FATP1 expression in female infants. DEHP exposure was negatively correlated with birth weight and gestational age in male infants. These results show that neonatal PAE exposure alters the mRNA expression of placental MTs and FATP1, which are related to fetal growth and development.

hero.3071083

Li, L; Liu, JC; Zhao, Y; Lai, FN; Yang, F; Ge, W; Dou, CL; Shen, W; Zhang, XF; Chen, H. (2015). Impact of diethylhexyl phthalate on gene expression and development of mammary glands of pregnant mouse. Histochem Cell Biol 144: 389-402. http://dx.doi.org/10.1007/s00418-015-1348-9.

The widely used diethylhexyl phthalate (DEHP) is a known endocrine disruptor that causes persistent alterations in the structure and function of female reproductive system, including ovaries, uterus and oviducts. To explore the molecular mechanism of the effect of DEHP on the development of mammary glands, we investigated the cell cycle, growth, proliferation and gene expression of mammary gland cells of pregnant mice exposed to DEHP. It was demonstrated, for the first time, that the mammary gland cells of pregnant mice treated with DEHP for 0.5-3.5days post-coitum had increased proliferation, growth rate and number of cells in the G2/S phase. The expression of cell proliferation-related genes was significantly altered after short time and low-dose DEHP treatment of mammary gland cells in vivo and in vitro. These findings showed adverse effects of DEHP on mammary gland cells in pregnant mice.

hero.3071027

Li, N; Chen, X; Zhou, X; Zhang, W; Yuan, J; Feng, J. (2015). The mechanism underlying dibutyl phthalate induced shortened anogenital distance and hypospadias in rats. J Pediatr Surg 50: 2078-2083. http://dx.doi.org/10.1016/j.jpedsurg.2015.08.046.

Purpose: The purpose of this study was to investigate the mechanism of dibutyl phthalate (DBP) induced hypospadias and shortened anogenital distance (AGD). Methods: AGD, hypospadias, and cryptorchidism incidence was observed in male offspring of DBP treated pregnant Wistar rats. Testicular development and testosterone levels of normal and DBP-treated rat embryos were compared. Results: Male offspring of 300 mg and 900 mg DBP-treated pregnant Wistar rats exhibited shortened average AGD compared with the control group. A 22.7% hypospadias incidence was observed in the 300 mg group, but no offspring with cryptorchidism were identified. In the 900 mg group, hypospadias and cryptorchidism incidence reached 43.5% and 17.4%, respectively. Between E15.5 and E17.5, the 300 mg group exhibited delayed testicular development and testosterone secretion. However, testicular development and testosterone secretion subsequently recovered. The 300 mg treated and control groups had similar measures after E19.5. Contrastingly, testicular development and testosterone secretion were significantly diminished throughout development in the 900 mg group. Exogenous testosterone partially counteracted DBP-induced changes in the reproductive organs of male offspring of DBP-treated rats. Conclusions: High-dose DBP exposure may induce testicular dysgenesis in rat embryos. Additionally, low-dose DBP may delay testicular development

and testosterone secretion during urethral development. This disruption may result in hypospadias. (c) 2015 Elsevier Inc. All rights reserved.

hero.3350245

Li, X; Chen, X; Hu, G; Li, L; Su, H; Wang, Y; Chen, D; Zhu, Q; Li, C; Li, J; Wang, M; Lian, Q; Ge, R. (2016). Effects of in Utero Exposure to Dicyclohexyl Phthalate on Rat Fetal Leydig Cells. Int J Environ Res Public Health 13. http://dx.doi.org/10.3390/ijerph13030246.

Dicyclohexyl phthalate (DCHP) is one of the phthalate plasticizers. The objective of the present study was to investigate the effects of DCHP on fetal Leydig cell distribution and function as well as testis development. Female pregnant Sprague Dawley dams orally received vehicle (corn oil, control) or DCHP (10, 100, and 500 mg/kg/day) from gestational day (GD) 12 to GD 21. At GD 21.5, testicular testosterone production, fetal Leydig cell number and distribution, testicular gene and protein expression levels were examined. DCHP administration produced a dose-dependent increase of the incidence of multinucleated gonocytes at 100 mg/kg. DCHP dose-dependently increased abnormal fetal Leydig cell aggregation and decreased fetal Leydig cell size, cytoplasmic size, and nuclear size at 10 mg/kg. DCHP reduced the expression levels of steroidogenesis-related genes (including Star, Hsd3b1, and Hsd17b3) and testis-descent related gene Insl3 as well as protein levels of 3β-hydroxysteroid dehydrogenase 1 (HSD3B1) and insulin-like 3 (INSL3) at 10 mg/kg. DCHP significantly inhibited testicular testosterone levels at 100 mg/kg. The results indicate that in utero exposure to DCHP affects the expression levels of fetal Leydig cell steroidogenic genes and results in the occurrence of multinucleated gonocytes and Leydig cell aggregation.

hero.3469478

Li, X; Shang, X; Luo, T; Du, X; Wang, Y; Xie, Q; Matsuura, N; Chen, J; Kadokami, K. (2016). Screening and health risk of organic micropollutants in rural groundwater of Liaodong Peninsula, China. Environ Pollut 218: 739-748. http://dx.doi.org/10.1016/j.envpol.2016.07.070.

Groundwater serves as a main drinking water source for rural residents in China. However, little is known regarding the pollution of organic micropollutants in groundwater that may pose health risks. In this study, more than 1300 organic micropollutants were screened in the groundwater samples collected from 13 drinking water wells distributed across five rural regions of Liaodong Peninsula in China. A total of 80 organic micropollutants including 12 polycyclic aromatic hydrocarbons, 11 alkanes, 9 pesticides, 7 substituted phenols, 7 perfluoroalkyl acids, 6 heterocyclic compounds, 5 alcohols, 5 phthalic acid esters, 5 pharmaceutical and personal care products, 3 ketones, 2 polychlorinated biphenyls (PCBs), 2 alkylbenzenes and 2 chlorinated benzenes were detected, with their total concentration of 32-1.510(4)ng/L. Noncarcinogenic and carcinogenic risks of a part of pollutants were assessed. Exposure through skin absorption and oral ingestion was considered in the assessment. Generally the risks are within the acceptable limits, except for that the carcinogenic risk at two sites in Jinzhou is higher than 10(-6). To the best of our knowledge, this is the first report on health risks of groundwater micropollutants in China.

hero.3350200

Li, X; Yin, P; Zhao, L. (2016). Phthalate esters in water and surface sediments of the Pearl River Estuary: distribution, ecological, and human health risks. Environ Sci Pollut Res 23: 19341-19349. http://dx.doi.org/10.1007/s11356-016-7143-x.

The Pearl River Estuary (PRE) is vulnerable due to the increasingly serious environmental pollution, such as phthalate esters (PAEs) contaminants, from the Pearl River Delta (PRD). The concentrations of six US Environmental Protection Agency (USEPA) priority PAEs in water and surface sediments collected from the PRD's six main estuaries in spring, summer, and winter 2013 were measured by GC-MS. Total PAEs (6PAEs) concentrations were from 0.5 to 28.1μg/L and from 0.88 to 13.6μg/g (dry weight (DW)) in water and surface sediments, respectively. The highest concentration was detected in summer. Higher concentrations of PAEs were found in Yamen (YM) and Humen (HM) areas than the other areas. Bis(2-ethylhexyl)phthalate (DEHP) and dibutyl phthalate (DBP) were the dominant PAEs in the investigated areas, contributing between 61 and 95% of the PAEs in water and from 85 to 98% in surface sediments. Based on risk quotients (RQs), DEHP posed greater ecological risks to the studied aquatic environments than other measured compounds. Little human health risk from the target PAEs was identified.

hero.3466581

Ling, J; Lopez-Dee, ZP; Cottell, C; Wolfe, L; Nye, D. (2016). Regulation of mRNA Translation Is a Novel Mechanism for Phthalate Toxicity. PLoS ONE 11: e0167914. http://dx.doi.org/10.1371/journal.pone.0167914.

Phthalates are a group of plasticizers that are widely used in many consumer products and medical devices, thus generating a huge burden to human health. Phthalates have been known to cause a number of developmental and reproductive disorders functioning as endocrine modulators. They are also involved in carcinogenesis with mechanisms less understood. To further understand the molecular mechanisms of phthalate toxicity, in this study we reported a new effect of phthalates on mRNA translation/protein synthesis, a key regulatory step of gene expression. Butyl benzyl phthalate (BBP) was found to directly inhibit mRNA translation in vitro but showed a complicated pattern of affecting mRNA translation in cells. In human kidney embryonic cell (HEK-293T), BBP increased cap-dependent mRNA translation at lower concentrations but showed inhibitory effect at higher concentrations. Cap-independent translation was not affected. On the other hand, mono (2-ethylhexyl) phthalate (MEHP) as a major metabolite of another important phthalate di (2-ethylhexyl) phthalate (DEHP) inhibited both can-dependent and -independent mRNA translation in vivo. In contrast, BBP and MEHP exhibited an overall promoting effect on mRNA translation in cancer cells. Mechanistic studies identified that the level and phosphorylation of eIF4E-BP (eIF4E binding protein) and the amount of eIF4GI in eIF4F complex were altered in accordance with the effect of BBP on translation. BBP was also identified to directly bind to eIF4E, providing a further mechanism underlying the regulation of mRNA by phthalate. At the cellular level BBP inhibited normal cell growth but slightly promoted cancer cells (HT29) growth. Overall, this study provides the first evidence that phthalates can directly regulate mRNA translation as a novel mechanism to mediate their biological toxicities.

hero.3469244

Liu, T; Jia, Y; Zhou, L; Wang, Q; Sun, D; Xu, J; Wu, J; Chen, H; Xu, F; Ye, L. (2016). Effects of Di-(2-ethylhexyl) Phthalate on the Hypothalamus-Uterus in Pubertal Female Rats. Int J Environ Res Public Health 13. http://dx.doi.org/10.3390/ijerph13111130.

The pollution of endocrine disruptors and its impact on human reproductive system have attracted much attention. Di-(2-ethylhexyl) phthalate (DEHP), an environmental endocrine disruptor, is widely used in food packages, containers, medical supplies and children's toys. It can cause diseases such as infertility, sexual precocity and uterine bleeding and thus arouse concerns from the society and scholars. The effect of DEHP on pubertal female reproductive system is still not well-studied. This study was to investigate the effects of DEHP on the hypothalamus-uterus in pubertal female rats, reveal the reproductive toxicity of DEHP on pubertal female rats and its mechanism, and provide scientific evidence for the evaluation of toxicity and toxic mechanism of DEHP on reproductive system. Forty-eight pubertal female rats were randomly divided into four groups and respectively administered via oral gavage 0, 250, 500, or 1000 mg/kg/d DEHP in 0.1 mL corn oil/20 g body weight for up to four weeks. Compared with control rats, the DEHP-treated rats showed: (1) higher gonadotropin-releasing hormone (GnRH) level in the hypothalamus; (2) higher protein levels of GnRH in the hypothalamus; and (3) higher mRNA and protein levels of GnRH receptor (GnRHR) in the uterus. Our data reveal that DEHP exposure may lead to a disruption in pubertal female rats and an imbalance of hypothalamus-uterus. Meanwhile, DEHP may, through the GnRH in the hypothalamus and its receptor on the uterus, lead to diseases of the uterus. DEHP may impose a negative influence on the development and functioning of the reproductive system in pubertal female rats.

hero.2510780

Liu, ZH; Li, EH; Xu, DL; Sun, WL; Hong, Y; Zhao, W; Xia, SJ; Jiang, JT. (2014). Genetic research and structural dysplasia assessment of anorectal malformations in neonatal male rats induced by di(n-butyl) phthalate. Environ Toxicol 31: 261-268. http://dx.doi.org/10.1002/tox.22040.

This study was the first to investigate the genetic abnormalities and structural dysplasia of anorectal malformations (ARMs) in male rats induced by di(n-butyl) phthalate (DBP). DBP was administered to timed-pregnant rats to establish the ARM rat model. The incidence of ARMs in male offspring was 39.5%. In neonatal period, decreased body weight and anogenital distance were observed. The general image and histological analysis of male offspring confirmed the presence of ARMs. Anatomical examination of the ARM male rats revealed the dysplasia in solid organs (heart-lung, liver, spleen, and kidney). The decreases of serum testosterone concentration and androgen receptor expression in terminal rectum were indicative of

the antiandrogenic effects of DBP. Moreover, significant decreased mRNA expressions of these androgen-related genes such as sonic hedgehog, Gli2, Gli3, bone morphogenetic protein 4, Wnt5a, Hoxa13, Hoxd13, fibroblast growth factor 10, and fibroblast growth factor receptor 2 were found in terminal rectum of the ARM male pubs. These results demonstrated that development of ARM rats was impaired by maternal exposure to DBP. The antiandrogenic effects of DBP disturbing the androgen-related signaling networks might play an important role in the occurrence of ARMs.

hero.3469542

Luo, S; Fang, HQ; Yang, H; Zhang, LS; Jia, XD. (2016). [Comparison of embryotoxicity of di(2-ethylhexyl) phthalate using mouse and human embryonic stem cell test models in vitro]. Zhonghua Yu Fang Yi Xue Za Zhi 50: 645-651.

OBJECTIVE: To establish a mouse embryonic stem cell test (mEST) model and human embryonic stem cell test (hEST) model, to evaluate the embryotoxicity of di(2-ethylhexyl) phthalate (DEHP).

METHODS: We developed mEST and hEST models according to the European Centre for the Validation of Alternative METHODS (ECVAM). We used penicillin G (PN-G) as the standard negative reference and 5-fluorouracil (5-FU) as the standard positive reference, respectively, to verify validity of the models. Based on model validity, mouse embryonic stem cells D3 (mESC-D3), mouse Balb/c-3T3 (3T3), and human embryonic stem cells H9 (hESC-H9) were administered different concentrations of DEHP (15.6, 31.2, 62.5, 125.0, 250.0, 500.0, and 1 000.0 μg/ml) for 7 days. A cell counting Kit-8 was used to detect the 50% inhibitory proliferation concentration (IC50) of mESC-D3 cells, 3T3 cells, and hESC-H9 with DEHP. mESC-D3 and hESC-H9 were treated with DEHP (15.6, 31.2, 62.5, 125.0, 250.0 μg/ml, and 500.0 μg/ml) for 10 days based on the cytotoxicity results. At day 10, the expression of cardiomyocyte differentiation gene alpha-myosin heavy chain (α-MHC) was detected by real-time PCR and the 50% inhibition of cardiomyocyte differentiation (ID50) determined. Based on the values of IC50 and ID50, functions , and could be calculated by three linear discriminant functions in the EST model and the embryotoxicity of DEHP described by comparing the three functions.

RESULTS: Nontrophoblast lineage both ES cells were cultured under optimal conditions and highly expressed hESC markers OCT4 , SSEA4, and TRA-1-60. The embryoid bodies formed were uniform in size and shape, and these results were highly repeatable. The PN-G and 5-FU results coincided with the prediction by ECVAM. Validation of our EST models was satisfactory. RESULTS of the three endpoints of DEHP in mEST were 197.3 μg/ml (IC50 3T3), 210.0 μg/ml (IC50 D3) and 246.8 μg/ml (ID50 D3). DEHP was evaluated to be a nonembryotoxic compound based on values of function (7.78), function (7.58) and function (-7.79). The three endpoints of DEHP in hEST were 195.4 μg/ml (IC50 3T3), 184.8 μg/ml (IC50 D3), and 84.3 μg/ml (ID50). By comparing the values of function (3.21), function (5.77), and function (-6.46), DEHP was evaluated to be weakly embryotoxic.

CONCLUSION: DEHP was determined to be a nonembryotoxic compound by mEST and weakly embryotoxic by hEST. Therefore, hEST is a more sensible model for the evaluation of DEHP embryotoxicity.

hero.3011344

Luongo, G; Östman, C. (2015). Organophosphate and phthalate esters in settled dust from apartment buildings in Stockholm. Indoor Air 26: 414-425. http://dx.doi.org/10.1111/ina.12217.

In this study, the occurrence of nine phthalate diesters (phthalates) and 14 organophosphorus flame retardants (PFRs) was investigated in 62 house dust samples collected from 19 buildings in Stockholm area during the year 2008. Eight phthalates were detected in almost all samples, with median concentrations ranging from 0.47μg/g to 449μg/g with di(2-ethylhexyl) phthalate being the most abundant compound. Twelve PFRs were detected with median concentrations ranging from 0.19μg/g to 11μg/g. Within this class of compounds, the most abundant were tris(2-chloroisopropyl) and tris(2-butoxyethyl) phosphate. Both classes of compounds were also measured in the air of the apartments, but no correlation between air and dust concentrations could be found. Based on these measurements, exposure, via house dust ingestion and air inhalation, was calculated for adults and toddlers, and compared to published limit values in order to estimate potential health risks. Inan extreme exposure scenario for toddlers, di(2-ethylhexyl) phthalate, tris(2-chloroethyl) phosphate, tris(2-butoxyethyl) phosphate, and tributyl phosphate were close to the reference dose for chronic oral exposure or the tolerable daily intake. Standard Reference Material SRM 2585 was used as a quality control sample, and the levels of diisononyl and diisodecyl phthalates were determined in this

material.

hero.3469280

Maghen, L; Shlush, E; Gat, I; Filice, M; Barretto, T; Jarvi, K; Lo, K; Gauthier-Fisher, AS; Librach, CL. (2016). Human umbilical perivascular cells: a novel source of MSCs to support testicular niche regeneration. Reproduction. http://dx.doi.org/10.1530/REP-16-0220.

The expansion of functional testicular biopsy-derived human spermatogonial stem cells (hSSC) ex-vivo may enable the restoration of fertility in pre-pubertal males having undergone gonadotoxic therapies or men with severe male factor infertility. Various somatic cells are known to regulate SSC homeostasis and spermatogenesis in the developing and adult testis. Prior attempts to recapitulate this niche demonstrated the requirement of feeder cells, such as endogenous testicular somatic cells, for germ cell expansion ex-vivo. However, this strategy has limitations for the expansion of hSSCs from tissue biopsies where spermatogenesis is absent or defective. Our aim was to evaluate first trimester human umbilical cord perivascular cells (FTM HUCPVCs), a novel source of mesenchymal stromal-like cells (MSCs), as potential human feeder cells for standardized hSSC expansion ex-vivo. Targeted RNA sequencing analysis demonstrated that CD90+ve FTM HUCPVCs expanded in vitro under germ cell culture conditions express a profile of targeted testicular-associated transcripts that is similar to cultured human CD90+ve testicular adherent cells (hTACs) and secrete LIF, FGF2 and BMP4, key growth factors known to regulate spermatogenesis. We also demonstrated that mitotically-inactivated FTM HUCPVCs support the expansion of mouse germ cells and putative SSCs ex-vivo, and that FTM HUCPVC transplantation promotes in vivo germ cell regeneration following mono-2- ethylhexyl phthalate (MEHP)-induced seminiferous tubule damage in a murine model, including a partial reconstitution of tubular cellular architecture and reestablishment of DAZL and acrosin+ve germ cell layers. Together, these data suggest that FTM HUCPVCs have phenotypical and functional properties that may support repair of the human testicular niche.

hero.3456499

Malakahmad, A; Law, MX; Ng, K, aWy; Sabariah, T, eh; Manan, A, bd. (2016). The Fate and Toxicity assessment of Polycyclic Aromatic Hydrocarbons (PAHs) in Water Streams of Malaysia. In Procedia Engineering. http://dx.doi.org/10.1016/j.proeng.2016.06.572.

Polycyclic aromatic hydrocarbons (PAHs) are pollutants released to the environment through natural and anthropogenic activities. PAHs if not being treated properly, are able to be transformed to various derivatives (daughters). There are possibilities that both PAHs and their daughter products to be toxic to environment and human. In this study, samples from influent of a water treatment plant (WTP) and effluent of sewage treatment plant (STP) were obtained to investigate presence of PAHs and their derivatives. Analysis of samples were conducted using Gas Chromatography Mass Spectrometry (GC/MS) and conversion formulation of the identified PAHs were found out. Furthermore, toxicity study carried out using guppy (Poecilia reticulate) to establish toxicity intensity of PAHs parents and daughters. The experiments were performed with three replicates using a total of 100 guppies for all definite tests through steady state method of acute toxicity test and mortality rates were investigated in 24, 48, 72 and 96 hours. Results indicated that phthalic acid and benzoic acid are significant compounds in both sampling points. Phthalic acid was found to be derived from Chrysene and Naphthalene whereas benzoic acid resulted from degradation of Fluoranthene. Mortality rates were 20% and 10%, in WTP influent and STP effluent, respectively. No mortality was observed in control tank which indicated accuracy of toxicity test. Although, the pollution levels in both samples did not produce 50% mortality, the findings could indicate the conditions affecting fish populations in prolonged duration. (C) 2016 The Authors. Published by Elsevier Ltd.

hero.3469402

Malik, AK; Aulakh, JS; Kaur, V. (2016). Capillary Electrophoretic Analysis of Classical Organic Pollutants. Methods Mol Biol 1483: 407-435. http://dx.doi.org/10.1007/978-1-4939-6403-1_20.

The synthesis and usage of a wide range of organic compounds have shown a considerable increase in the past few decades. Many of these compounds are potential pollutants for the environment. They differ from each other in their chemical structure and properties. Correspondingly different separation strategies are required for their separation. There is need to assess the human exposure to these chemicals and to identify and develop analytical methods for their identification. In this chapter we have presented some methods for

the separation and the analysis of the organic pollutants like dyes, phenolic pollutants, phthalates, endocrine disrupting chemicals, polycyclic aromatic hydrocarbon, explosives, agricultural pesticides, and toxins.

hero.3479530

Mallozzi, M; Bordi, G; Garo, C; Caserta, D. (2016). The effect of maternal exposure to endocrine disrupting chemicals on fetal and neonatal development: A review on the major concerns [Review]. Birth Defects Res C Embryo Today 108: 224-242. http://dx.doi.org/10.1002/bdrc.21137.

There is a widespread exposure of general population, including pregnant women and developing fetuses, to the endocrine disrupting chemicals (EDCs). These chemicals have been reported to be present in urine, blood serum, breast milk, and amniotic fluid. Endocrine disruptions induced by environmental toxicants have placed a heavy burden on society, since environmental exposures during critical periods of development can permanently reprogram normal physiological responses, thereby increasing susceptibility to disease later in life-a process known as developmental reprogramming. During development, organogenesis and tissue differentiation occur through a continuous series of tightly-regulated and precisely-timed molecular, biochemical, and cellular events. Humans may encounter EDCs daily and during all stages of life, from conception and fetal development through adulthood and senescence. Nevertheless, prenatal and early postnatal windows are the most critical for proper development, due to rapid changes in system growth. Although there are still gaps in our knowledge, currently available data support the urgent need for health and environmental policies aimed at protecting the public and, in particular, the developing fetus and women of reproductive age. Birth Defects Research (Part C) 108:224-242, 2016. 2016 Wiley Periodicals, Inc.

hero.3479522

Mao, Y, unF; Li, Z; He, Y, aL; Tao, W, enQ. (2016). CFD analysis of SVOC mass transfer in different chambers. Int J Heat Mass Tran 99: 613-621. http://dx.doi.org/10.1016/j.ijheatmasstransfer.2016.04.006.

Semi-volatile organic compound (SVOC) in indoor environment is an important research topic because of their wide use and persistent effect on human health. SVOC chambers have been continually improved to study the mass transfer characteristics in indoor environment. CFD method is used in the present paper to study the effect on mass transfer, especially on steady time by velocity field from the comparison of SVOC mass transfer in two different SVOC chambers (A and B). The results indicate that the variance of air flow in small range strongly affects the steady concentration and has no obvious effect on steady time. Sorption ability itself has great impact on steady time. The great reduction of steady time in Chamber B is the combined effect of sorption and velocity field. The velocity field resulted from the special structure of Chamber B leads to a stronger convective mass transfer resistance, and hence causes a weaker effective sorption. Therefore, the less steady time in Chamber B is the result of weaker effective sorption besides a less sorption area of Chamber B than Chamber A. (C) 2016 Elsevier Ltd. All rights reserved.

hero.3469538 REVIEW

Mariana, M; Feiteiro, J; Verde, I; Cairrao, E. (2016). The effects of phthalates in the cardiovascular and reproductive systems: A review [Review]. Environ Int 94: 758-776. http://dx.doi.org/10.1016/j.envint.2016.07.004.

Every year millions of tons of plastic are produced around the world and humans are increasingly exposed to them. This constant exposure to plastics has raised some concerns against human health, particularly when it comes to phthalates. These compounds have endocrine-disrupting properties, as they have the ability to bind molecular targets in the body and interfere with hormonal function and quantity. The main use of phthalates is to give flexibility to polyvinyl chloride (PVC) polymers. Phthalates are found in a variety of industrial and consumer products, and as they are not covalently bound to the plastic, phthalates contaminate the environment from which human exposure occurs. Studies in human and animal populations suggest a correlation between phthalate exposure and adverse health outcomes, particularly at the reproductive and cardiovascular systems, however there is much less information about the phthalate toxicity of the later. Thus, the main purpose of this review is to present the studies relating the effects already stated of phthalates on the cardiovascular and reproductive systems, and also present the link between these two systems.

hero.3350259

Martins, K; Hagedorn, B; Ali, S; Kennish, J; Applegate, B; Leu, M; Epp, L; Pallister, C; Zwollo, P. (2016). Tissue Phthalate

Levels Correlate With Changes in Immune Gene Expression in a Population of Juvenile Wild Salmon. Arch Environ Contam Toxicol 71: 35-47. http://dx.doi.org/10.1007/s00244-016-0283-7.
Phthalates have detrimental effects on health and have been shown to dysregulate the immune system of mammals, birds, and fish. We recently reported that di(2-ethylhexyl) phthalate exposure reduces the abundance and inhibits the proliferation of rainbow trout (Oncorhynchus mykiss) IgM(+) B lymphocytes and expression of secreted immunoglobulin heavy-chain mu transcripts in an in vitro culture system. We proposed that phthalates act as immunomodulators by modifying the normal B cell-activation pathways by accelerating B cell differentiation while suppressing plasmablast expansion, thus resulting in fewer IgM-secreting plasma cells. This hypothesis was tested here in an in vivo field study of juvenile Dolly Varden (Salvelinus malma) from a plastic-polluted lake in the Gulf of Alaska. Fish tissues were analyzed for both phthalate levels using liquid chromatography-coupled tandem mass spectrometry and for changes in immune gene expression using reverse transcriptase-real time polymerase chain reaction. Results showed that fish with higher tissue levels of di(2-ethylhexyl) phthalate, di(n-butyl) phthalate, and/or dimethyl phthalate expressed significantly fewer secreted and membrane-bound immunoglobulin heavy-chain mu and Blimp1 transcripts in their hematopoietic tissue. This suggests that in vivo uptake of phthalates in fish changes the expression of B cell-specific genes. Chronic exposure to phthalates likely dysregulates normal B-lymphoid development and antibody responses in salmonids and may increase susceptibility to infection. Given the conserved nature of B-lineage cells in vertebrate animals, other marine species may be similarly affected by chronic phthalate exposure.

hero.3360788

Mcclafferty, H. (2016). Environmental Health: Children's Health, a Clinician's Dilemma. Curr Probl Pediatr Adolesc Health Care 46: 184-189. http://dx.doi.org/10.1016/j.cppeds.2015.12.003.
Few pediatricians receive training in environmental health, yet accumulating research shows that a disproportionate burden of exposure from environmental toxicants (man-made contaminants) is borne by children, adolescents, and the developing fetus. This is explained in part because of childrens vulnerability to environmental-toxicants based on socioeconomic status, body surface area, metabolism, and potential transfers via placenta and breast milk. Public concern about toxicants affecting children in air, land, water, food, and beverages places pediatricians in the challenging position of being expected to knowledgably answer questions about environmental exposures while lacking sufficient training in the field. Surveys show pediatricians have high interest in environmental topics, yet feel a low sense of self-efficacy regarding patient education and lack evidence-based treatment guidelines and other effective educational tools. The goal of this article is to provide an overview of selected toxicants relevant to pediatric health, review practical suggestions to reduce or eliminate children's exposures, and introduce resources for taking an environmental health history to better prepare pediatricians and other clinicians caring for children to decrease harmful exposures in infants, children, and adolescents.

hero.3479517

Mendiola, J; Oñate-Celdrán, J; Samper-Mateo, P; Arense-Gonzalo, JJ; Torres-Roca, M; Sánchez-Rodríguez, C; García-Escudero, D; Fontana-Compiano, LO; Eisenberg, ML; Swan, SH; Torres-Cantero, AM. (2016). Comparability and reproducibility of adult male anogenital distance measurements for two different methods. Andrology 4: 626-631. http://dx.doi.org/10.1111/andr.12202.
The distance from the genitals to the anus, anogenital distance, reflects androgen concentration during prenatal development in mammals. The use of anogenital distance in human studies is still very limited and the quality and consistency of measurements is an important methodological issue. The aim of this study was to assess the feasibility and reproducibility of adult male anogenital distance measurements by two different methods. All men were attending an outpatient clinic at a university hospital and underwent an andrological examination and completed a brief questionnaire. Two variants of anogenital distance [from the anus to the posterior base of the scrotum (AGDAS) and to the cephalad insertion of the penis (AGDAP)] by two methods (lithotomy or frog-legged position) were assessed in 70 men. Within and between coefficient of variations, intra-class correlation coefficients, two-way repeated-measures analysis of variance, and scatter and Bland-Altman plots were calculated. The two methods produced similar values for AGDAP but different estimates for AGDAS . Nonetheless, the overall agreement (ICC0.80) was acceptable for both measures. Therefore, both methods are internally consistent and adequate for epidemiological studies, and may be

used depending on the available medical resources, clinical setting, and populations.

hero.3479526

Mendiola, J; Sánchez-Ferrer, ML; Jiménez-Velázquez, R; Cánovas-López, L; Hernández-Peñalver, AI; Corbalán-Biyang, S; Carmona-Barnosi, A; Prieto-Sánchez, MT; Nieto, A; Torres-Cantero, AM. (2016). Endometriomas and deep infiltrating endometriosis in adulthood are strongly associated with anogenital distance, a biomarker for prenatal hormonal environment. Hum Reprod 31: 2377-2383. http://dx.doi.org/10.1093/humrep/dew163. STUDY QUESTION: Is the length of the anogenital distance (AGD), a biomarker of the in-utero prenatal hormonal environment, associated with the presence of endometriomas and deep infiltrating endometriosis (DIE)?

SUMMARY ANSWER: Shorter AGD is associated with presence of endometriomas and DIE.

WHAT IS KNOWN ALREADY: It is debated whether hormonal exposure to estrogens in utero may be a risk factor for endometriosis in adulthood. AGD is a biomarker of prenatal hormonal environment and observational studies have shown an association between AGD and reproductive parameters in both sexes.

STUDY DESIGN, SIZE, DURATION: This case-control study of 114 women with endometriosis (endometriomas and/or DIE) and 105 controls was conducted between September 2014 and May 2015.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Cases were attending the Endometriosis Unit of the Hospital. Prevalent as well as incident cases, diagnosed by transvaginal ultrasound (TVUS), were included. Controls were women without endometriosis attending the gynecological outpatient clinic for routine gynecological exams. Participants completed health questionnaires, followed physical and gynecological examinations, including TVUS. Measurements from the anterior clitoral surface to the upper verge of the anus (AGDAC), and from the posterior fourchette to the upper verge of the anus (AGDAF) were obtained in all subjects. Unconditional multiple logistic regression was used to estimate the association between AGD measurements and presence of endometriomas and/or DIE while accounting for important confounders and covariates, including age, body mass index, vaginal delivery or episiotomy.

MAIN RESULTS AND THE ROLE OF CHANCE: AGDAF was related to presence of endometriomas and/or DIE. For all cases of endometriosis (endometriomas and DIE), women in the lowest tertile of the AGDAF distribution, compared with the upper tertile, were 7.6-times (95% CI 2.8-21.0; P-trend < 0.001) more likely to have endometriosis. With regard to DIE, women with AGDAF below the median, compared with those with AGDAF above the median, were 41.6-times (95% CI 3.9-438; P-value = 0.002) more likely to have endometriosis.

LIMITATIONS, REASONS FOR CAUTION: In case-control studies, information and selection bias has to be ruled out. Physicians conducting the measurement were blind to the status of the patients. Controls came from the same population as the cases. We adjusted for known and suspected confounders and covariates, but the possibility of residual confounding or chance findings should always be considered. As with all observational studies, causal inference is limited.

WIDER IMPLICATIONS OF THE FINDINGS: This study suggests that endometriosis, especially the DIE, might have a prenatal origin that may be traced back to the hormonal milieu in which the fetus develops.

STUDY FUNDING/COMPETING INTEREST: This work was supported by the Ministry of Economy and Competitiveness, ISCIII (AES), grant no. PI13/01237 and the Seneca Foundation, Murcia Regional Agency of Science and Technology, grant no. 19443/PI/14. The authors have no competing interests to declare.

TRIAL REGISTRATION NUMBER: Not applicable.

hero.3455686

Miao, Y; Wang, R; Lu, C; Zhao, J; Deng, Q. (2016). Lifetime cancer risk assessment for inhalation exposure to di(2-ethylhexyl) phthalate (DEHP). Environ Sci Pollut Res. http://dx.doi.org/10.1007/s11356-016-7797-4. The plasticizer di(2-ethylhexyl) phthalate (DEHP) is ubiquitous in the environment and considered as carcinogen; however, the carcinogenic risk of human exposure to DEHP in the air via inhalation is lacking. A probabilistic incremental lifetime cancer risk (ILCR) model was implemented to quantitatively estimate the potential cancer risk of DEHP via human inhalation by using Monte Carlo simulation. We assessed the cancer risk in different age groups (children, adolescents, and adults) exposed to different DEHP concentrations (background low, indoor moderate, and occupational high) for different durations (2, 8, and 20years). Results showed that the cancer risk of exposure to DEHP was below the acceptable limit (10(-6)) in the ambient air but was serious in indoor and occupational environments even at short exposure duration (2years). The

cancer risk of DEHP via inhalation in children was lower than that in adolescents and adults, but the risk in children via dermal and oral exposure to indoor dust and soft PVC toys should be considered. Sensitivity analysis indicated that the exposure concentration of DEHP was the strongest factor that influenced ILCR. Our work provides the evidence of cancer risk of DEHP via inhalation and highlights the risk in indoor and occupational environments.

hero.3469199

Minatoya, M; Araki, A; Miyashita, C; Sasaki, S; Goto, Y; Nakajima, T; Kishi, R. (2017). Prenatal di-2-ethylhexyl phthalate exposure and cord blood adipokine levels and birth size: The Hokkaido study on environment and children's health. Sci Total Environ 579: 606-611. http://dx.doi.org/10.1016/j.scitotenv.2016.11.051.

Di-2-ethylhexyl phthalate (DEHP) is one of the most widely used phthalates. Metabolites of DEHP are detectable in majority of the population. Findings on adverse health outcomes, particularly birth weight in association with prenatal exposure to DEHP remain equivocal. Besides, there is insufficient evidence to address influence on metabolic function from epidemiological studies. Thus, our objective was to investigate cord blood adipokine levels and birth size in association with prenatal DEHP exposure in prospective birth cohort study. Mono-2-methylhexyl phthalate (MEHP), primary metabolite of DEHP was determined as exposure by using maternal blood sample of 3rd trimester. Leptin and adiponectin levels in cord blood were measured as markers of metabolic function. Birth weight and length were obtained from birth record. Association between maternal MEHP levels and cord blood adiponectin and leptin levels, birth weight and ponderal index (PI) were examined for 167 mother-child pairs who had both MEHP and cord blood adipokine measurements. The median MEHP level was 8.81ng/ml and the detection rate was 100%. There was no sex difference in MEHP levels. Both leptin and adiponectin levels were higher in girls than in boys. MEHP level was positively associated with adiponectin level among boys and was negatively associated with leptin level among girls. MEHP level were negatively associated with PI only in girls and this could be due to decreased leptin level. This study suggested that prenatal DEHP exposure may be associated with cord blood adipokine and birth size. The influence potentially be sex-specific and could be more significant in girls.

hero.3479525

Mínguez-Alarcón, L; Gaskins, AJ; Chiu, YH; Souter, I; Williams, PL; Calafat, AM; Hauser, R; Chavarro, JE; team, ES. (2016). Dietary folate intake and modification of the association of urinary bisphenol A concentrations with in vitro fertilization outcomes among women from a fertility clinic. Reprod Toxicol 65: 104-112. http://dx.doi.org/10.1016/j.reprotox.2016.07.012.

Experimental data in rodents suggest that the effects of bisphenol A (BPA) on oocyte development may be modified by dietary methyl donors. Whether the same interaction exists in humans is unknown. We evaluated whether intake of methyl donors modified the associations between urinary BPA concentrations and treatment outcomes among 178 women who underwent 248 IVF cycles at a fertility center in Boston between 2007 and 2012. Participants completed a validated food frequency questionnaire and provided up to two urine samples per treatment cycle. High urinary BPA concentrations were associated with a 66% lower probability of implantation (p=0.007) among women who consumed <400μg/day of food folate, but not among women consuming 400μg/day (21% higher probability of implantation, p=0.18) (p,interaction=0.04). A similar pattern was observed for probability of clinical pregnancy (p,interaction=0.07) and live birth (p,interaction=0.16). These results are consistent with previous animal data but further evaluation in other human populations is needed.

hero.3469340

Mínguez-Alarcón, L; Souter, I; Chiu, YH; Williams, PL; Ford, JB; Ye, X; Calafat, AM; Hauser, R; Team, ES. (2016). Urinary concentrations of cyclohexane-1,2-dicarboxylic acid monohydroxy isononyl ester, a metabolite of the non-phthalate plasticizer di(isononyl)cyclohexane-1,2-dicarboxylate (DINCH), and markers of ovarian response among women attending a fertility center. Environ Res 151: 595-600. http://dx.doi.org/10.1016/j.envres.2016.08.012.

Di(isononyl)cyclohexane-1,2-dicarboxylate (DINCH), a non-phthalate plasticizer, was introduced commercially in 2002 as an alternative to ortho-phthalate esters because of its favorable toxicological profile. However, the potential health effects from DINCH exposure remain largely unknown. We explored the associations between urinary concentrations of metabolites of DINCH on markers of ovarian response

among women undergoing in vitro fertilization (IVF) treatments. Between 2011 and 2015, 113 women enrolled a prospective cohort study at the Massachusetts General Hospital Fertility Center and provided up to two urine samples prior to oocyte retrieval. The urinary concentrations of two DINCH metabolites, cyclohexane-1,2-dicarboxylic acid monohydroxy isononyl ester (MHiNCH) and cyclohexane-1,2-dicarboxylic acid monocarboxyisooctyl ester (MCOCH), were quantified by isotope dilution tandem mass spectrometry. We used generalized linear mixed models to evaluate the association between urinary metabolite concentrations and markers of ovarian response, accounting for multiple IVF cycles per woman via random intercepts. On average, women with detectable urinary MHiNCH concentrations, as compared to those below LOD, had a lower estradiol levels (-325 pmol/l, p=0.09) and number of retrieved oocytes (-1.8, p=0.08), with a stronger association among older women. However, urinary MHiNCH concentrations were unrelated to mature oocyte yield and endometrial wall thickness. In conclusion, we found suggestive negative associations between urinary MHiNCH concentrations and peak estradiol levels and number of total oocyte yields. This is the first study evaluating the effect of DINCH exposure on human reproductive health and raises the need for further experimental and epidemiological studies to better understand the potential effects of this chemical on health.

hero.3456406

Mitro, SD; Dodson, RE; Singla, V; Adamkiewicz, G; Elmi, AF; Tilly, MK; Zota, AR. (2016). Consumer Product Chemicals in Indoor Dust: A Quantitative Meta-analysis of U.S. Studies. Environ Sci Technol 50: 10661-10672. http://dx.doi.org/10.1021/acs.est.6b02023.

Indoor dust is a reservoir for commercial consumer product chemicals, including many compounds with known or suspected health effects. However, most dust exposure studies measure few chemicals in small samples. We systematically searched the U.S. indoor dust literature on phthalates, replacement flame retardants (RFRs), perfluoroalkyl substances (PFASs), synthetic fragrances, and environmental phenols and estimated pooled geometric means (GMs) and 95% confidence intervals for 45 chemicals measured in 3 data sets. In order to rank and contextualize these results, we used the pooled GMs to calculate residential intake from dust ingestion, inhalation, and dermal uptake from air, and then identified hazard traits from the Safer Consumer Products Candidate Chemical List. Our results indicate that U.S. indoor dust consistently contains chemicals from multiple classes. Phthalates occurred in the highest concentrations, followed by phenols, RFRs, fragrance, and PFASs. Several phthalates and RFRs had the highest residential intakes. We also found that many chemicals in dust share hazard traits such as reproductive and endocrine toxicity. We offer recommendations to maximize comparability of studies and advance indoor exposure science. This information is critical in shaping future exposure and health studies, especially related to cumulative exposures, and in providing evidence for intervention development and public policy.

hero.3479502

Mo, J, iX; Li, SS; Xu, W, eihui; Yu, Z, hidan; Wang, Z, hiG. (2016). BIODEGRADATION OF DIMETHYL PHTHALATE BY BACILLUS SP M-7 ISOLATED FROM SALINE-ALKALI SOIL AND ENHANCED DEGRADATION RATE USING RESPONSE SURFACE METHODOLOGY. Fresen Environ Bull 25: 1395-1405.

Large areas of saline-alkaline land in China are polluted by phthalic acid esters (PAEs). Among the PAEs, dimethyl phthalate (DMP) is an important synthetic organic that seriously threatens human health. The objectives of this study are to investigate the biodegradation kinetics of DMP by a new bacterium, Bacillus sp. M-7, isolated from saline-alkaline soil and to optimize the degradation rate of DMP using response surface methodology (RSM). Bacillus sp. M-7 can utilize DMP as its sole carbon and energy source under high salinity and alkaline conditions. Results show that the biodegradation process fits well with a first-order kinetic model and the half-life of DMP degradation ranges from 0.8682 to 2.2696 d as the initial DMP concentration varies from 10 to 800 mg/L. The separate effects of pH, temperature, Na+ level and Fe2+ level on the kinetics of DMP biodegradation were also determined. Results of batch experiments show that the four environmental factors strongly affect DMP degradation. The DMP degradation rate decreases significantly at the levels > pH 9.0, > 40 degrees C, > 6 g/L Na+ or > 40 mg/L Fe2+. After optimization of the four factors using RSM, the DMP degradation rate increases by 32.4% than that under basic conditions and is maximized to 2.2771 mg/(L.h). This is the first report on the statistical optimization of DMP degradation rate.

hero.3470397

Moreau-Guigon, E; Alliot, F; Gasperi, J; Blanchard, M; Teil, MJ; Mandin, C; Chevreuil, M. (2016). Seasonal fate and gas/particle partitioning of semi-volatile organic compounds in indoor and outdoor air. Atmos Environ 147: 423-433. http://dx.doi.org/10.1016/j.atmosenv.2016.10.006.

Fifty-eight semi-volatile organic compounds (SVOCs) were investigated simultaneously in three indoor (apartment, nursery and office building) and one outdoor environment in the centre of Paris (France). All of these compounds except tetrabromobisphenol A were quantified in the gaseous and particulate phases in all three environments, and at a frequency of 100% for the predominant compounds of each SVOC class. Phthalic acid esters (PAEs) were the most abundant group (di-iso-butyl phthalate: 29-661 ng m(-3), diethyl phthalate: 15-542 ng m(-3)), followed by 4-nonylphenol (1.4-81 ng m(-3)), parabens (methylparaben: 0.03-2.5 ng m(-3)), hexachlorobenzene (HCB) (0.002-0.26 ng m(-3)) and pentachlorobenzene (PeCB) (0.001-0.23 ng m(-3)). Polycyclic aromatic hydrocarbons (as Sigma 8PAHs) ranged from 0.17 to 5.40 ng m(-3), polychlorinated biphenyls (as Sigma 7PCBi) from 0.06 to 4.70 ng.m(3) and polybromodiphenyl ethers (as Sigma 8PBDEs) from 0.002 to 0.40 ng m(-3). For most pollutants, significantly higher concentrations were observed in the nursery compared to the apartment and office. Overall, the indoor air concentrations were up to ten times higher than outdoor air concentrations. Seasonal variations were observed for PAEs, PCBs and PAHs. SVOCs were predominantly identified in the gaseous phase (>90%), except for some high-molecular-weight PAEs, PAHs and PCBs. (C) 2016 Elsevier Ltd. All rights reserved.

hero.3469353

Morgan, M; Deoraj, A; Felty, Q; Roy, D. (2016). Environmental estrogen-like endocrine disrupting chemicals and breast cancer. Mol Cell Endocrinol. http://dx.doi.org/10.1016/j.mce.2016.10.003.

BACKGROUND: Estrogen-mimicking endocrine disruptors (EEDs) such as polychlorinated biphenyls (PCBs), bisphenol A (BPA), and phthalates have been found ubiquitously throughout our environment. Although exposure to EEDs has the ability to interfere with endocrine control of reproductive function and development in both humans and wildlife, inconsistent reports have made it difficult to draw conclusions concerning the hypothesized increased risk of breast cancer associated with EEDs.

OBJECTIVES: The purpose of this study was to examine the cross-sectional relationship between exposure to PCBs, BPA or phthalates; and risk of breast cancer in U.S. women using the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES) data between 1999 and 2004.

METHODS: We analyzed data from female participants (20 years of age and older) collected by NHANES between 1999 and 2004 for exposure assessment based on lipid adjusted serum levels of 6 individual PCB congeners (PCB 074, 099, 118, 138, 153, and 180), the sum of dioxin-like PCBs (074 and 118), and the sum of non-dioxin-like PCBs (099+138+153+187). Levels of urinary BPA and seven phthalate metabolites mono-n-butyl phthalate (MnBP), mono-isobutyl phthalate (MiBP), mono-ethyl phthalate (MEP), mono-(3-caroxypropyl) phthalate (MCPP), mono-benzyl phthalate (MZP), and three metabolites of di (2-ehtylhexyl) phthalate (DEHP): [mono-2-ethylhexyl phthalate (MEHP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), and mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP)] were obtained from the 2003-2010 yearly survey cycles in participants aged 6 years and older. Assessments of EEDs or their metabolites were analyzed in conjunction with medical and reproductive health questionnaire data. Age, race/ethnicity, age at menarche, body mass index (BMI; kg/m(2)), and lactation were considered as potential confounders in our final models. Geometric means (GM) were calculated to compare PCB, BPA or phthalate concentrations in women who self-reported a breast cancer diagnosis versus women who self-reported never being diagnosed with breast cancer. Logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CI) for the association between PCB, BPA or phthalate measurements and breast cancer.

RESULTS: In age, race/ethnicity, and BMI adjusted models, PCB138 was the only congener found to be significantly associated with breast cancer [OR of 3.16; 95% CI: 1.14-8.76]. We also found the sum of non-dioxin-like PCBs to be significantly associated with breast cancer [OR of 1.14; 95% CI: 1.00-1.29]. Risk of breast cancer, however, was not found to be significantly associated with phthalate, phthalate metabolites, and BPA in unadjusted or adjusted logistic regression models.

CONCLUSIONS: Our results suggest a link between environmental exposures to PCB 138 and breast cancer. There were no significant associations between phthalates or BPA and breast cancers. These findings should be interpreted with caution because of the use of cross-sectional self-reported data and a small sample size of breast cancer subjects. Nonetheless, our

finding emphasizes a need of comprehensive environmental molecular epidemiologic study to determine the potential role of environmental exposures to PCBs, phthalates, and BPA in the development of breast cancer.

hero.3469207

Morrison, GC; Weschler, CJ; Bekö, G. (2016). Dermal uptake of phthalates from clothing: Comparison of model to human participant results. Indoor Air. http://dx.doi.org/10.1111/ina.12354.

In this research, we extend a model of transdermal uptake of phthalates to include a layer of clothing. When compared with experimental results, this model better estimates dermal uptake of diethylphthalate and di-n-butylphthalate (DnBP) than a previous model. The model predictions are consistent with the observation that previously exposed clothing can increase dermal uptake over that observed in bare-skin participants for the same exposure air concentrations. The model predicts that dermal uptake from clothing of DnBP is a substantial fraction of total uptake from all sources of exposure. For compounds that have high dermal permeability coefficients, dermal uptake is increased for (i) thinner clothing, (ii) a narrower gap between clothing and skin, and (iii) longer time intervals between laundering and wearing. Enhanced dermal uptake is most pronounced for compounds with clothing-air partition coefficients between 10(4) and 10(7) . In the absence of direct measurements of cotton cloth-air partition coefficients, dermal exposure may be predicted using equilibrium data for compounds in equilibrium with cellulose and water, in combination with computational methods of predicting partition coefficients.

hero.3324167

Motohashi, M; Wempe, MF; Mutou, T; Okayama, Y; Kansaku, N; Takahashi, H; Ikegami, M; Asari, M; Wakui, S. (2016). In utero-exposed di(n-butyl) phthalate induce dose dependent, age-related changes of morphology and testosterone-biosynthesis enzymes/associated proteins of Leydig cell mitochondria in rats. J Toxicol Sci 41: 195-206. http://dx.doi.org/10.2131/jts.41.195.

Female pregnant Sprague-Dawley rats were intragastrically (ig) administered di(n-butyl) phthalate (DBP) at four doses (0, 10, 50 and 100 mg/kg) during gestation days (GD) 12-21 (n = 5 per group). The age-related morphological changes of Leydig cell mitochondrion (LC-Mt) and testosterone biosynthesis enzymes/associated genes/proteins expression levels were investigated. As compared to the control (no DBP), the 10 mg, and 50 mg DBP dose groups, the 100 mg DBP dose group at weeks 5 and 7 showed a significant amount of small LC-Mt. Thereafter, from weeks 9 to 17, the LC-Mt size and quantity in the 100 mg DBP dose group increased and became statistically similar to the other dose groups; hence, dose and time-dependent LC-Mt changes were observed. Throughout the study, the 100 mg DBP dose group had significantly lower testosterone levels. In addition, the 100 mg DBP dose group displayed lower StAR (StAR, steroidogenic acute regulatory protein) and P450scc (CYP11a1, cholesterol side-chain cleavage enzyme) levels at weeks 5 and 7, but they became statistically similar to all other dose groups at weeks 9 to 17; in contrast, the SR-B1 (Sarb1, scavenger receptor class B member 1) levels were similar for all DBP dose groups. The rats in utero 100 mg DBP /kg/day (GD 12-21) exposure results from this study indicate a dose-dependent, age-related morphological change in LC-Mt which are linked to reductions in testosterone biosynthesis genes / proteins expression, specifically StAR and P450scc.

hero.3070922

Motohashi, M; Wempe, MF; Mutou, T; Takahashi, H; Kansaku, N; Ikegami, M; Inomata, T; Asari, M; Wakui, S. (2015). Male rats exposed in utero to di(n-butyl) phthalate: age-related changes in Leydig cell smooth endoplasmic reticulum and testicular testosterone-biosynthesis enzymes/proteins. Reprod Toxicol 59: 139-146. http://dx.doi.org/10.1016/j.reprotox.2015.12.001.

This study investigated the age-related (i.e. weeks 5, 7, 9, 14 and 17) morphological changes of Leydig cell smooth endoplasmic reticulum (LCs-ER) and testicular testosterone biosynthesis/protein expression in rats in utero exposed to di(n-butyl) phthalate (DBP) (intragastrically; 100mg/kg/day) on days 12-21 post-conception. Ultrastructural observations revealed the LCs-ER of the DBP group were non-dilated until peri-puberty, and thereafter decreased and disappeared. RT-PCR and Western blotting analyses revealed that StAR and P450scc levels in the DBP group were significantly lower at 5 and 7 weeks compared with the vehicle group but became similar during weeks 9 to 17. Although 3β-HSD, P450c17, and 17β-HSD levels of mRNA and protein in the DBP group were similar to the vehicle control group at 5 and 7 weeks of age, they

were significantly lower during weeks 9 to 17. In utero DBP exposure results in age-related LCs-ER changes corresponding to reduction of testicular testosterone biosynthesis enzymes/associated proteins.

hero.3472278

Mu, Y, uT; Chen, L, i; He, Y, aL; Tao, W, enQ. (2016). Pore-scale modelling of dynamic interaction between SVOCs and airborne particles with lattice Boltzmann method. Build Environ 104: 152-161. http://dx.doi.org/10.1016/j.buildenv.2016.05.002.

Semivolatile organic compounds (SVOCs) can be easily adsorbed on the suspended particulate matter (PM), and the exchange of SVOCs across the air-particle interface is crucial for the determination of their exposure on human. In the present study, an airborne. particle with a diameter of 2.5 mu m is fully reconstructed and applied to investigate the SVOCs transport mechanism and the adsorption/desorption process. The pore size distribution of the particle is statistically estimated, based on which Knudsen and Fick difftision mechanisms are considered. The sorption process between the adsorbed SVOCs on the element carbon (EC) and SVOCs in organic matter (OM) is performed with Langmuir-isotherm model. The effective diffusivity in particle is numerically predicted and compared with the existing empirical study. The influences of the equilibrium sorption constant and the volume fraction of organic matter and carbon on the dynamic interaction process are also explored. Results show that the effective diffusivity of the PM particle with low porosity predicted with the present model is much lower than that adopted by the Bruggeman equation. The amount of adsorbed di-2-ethyhexyl phthalate (DEHP) on EC is predominant compared with the gas phase in pores and dissolved phase in PM. The total-amount of DEHP transporting from air to the PM particle is highly influenced by the equilibrium sorption constant and the volume fraction of EC. The influence of Volume fraction of OM on the total amount of adsorbed DEHP is slight. (C) 2016 Elsevier Ltd. All rights reserved.

hero.3469309

Müllerová, D; Bouchalová, V; Matějková, D; Kovářová, K; Svačina, Š; Vrbík, K; Pavloušková, J; Dvořáková, J; Müller, L. (2016). Phthalates exposure indicators determined by urinary phthalate metabolites in healthy non-obese Czech adults: FANTOM study. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 33: 1817-1825. http://dx.doi.org/10.1080/19440049.2016.1241898.

It is assumed that human exposure to phthalates may be associated with adverse health effects. The indicators of urinary phthalate metabolite concentrations in healthy adults are limited. In this study, the phthalate metabolites concentrations were detected from 24-h urine collection in non-obese Czech adults (n=201). Each participant filled in an 80-item questionnaire (FANTOM-SQ 2013) regarding the outdoor and indoor sources of phthalates, the use of personal care products and food intake sources. The concentrations of 15 phthalates metabolites were analysed following enzymatic cleavage of the glucuronide using ultra-high-performance liquid chromatography-electrospray ionisation tandem mass spectrometry (UHPLC-ESI-MS/MS). The indicators of chronic or acute exposure phthalate-containing materials were identified. It is shown that higher fruit consumption was positively and significantly associated with a higher level of total 15 urinary phthalates biomarkers (p <0.001). Regular meat consumption showed a negative significant association with total 15 phthalates metabolites (p <0.01). The use of personal care products was significantly and positively correlated with monoethyl phthalate urine concentrations (p <0.05). The analysis of the dietary behaviour and personal care products use in the Czech non-obese population showed it to be a predictable tool in the level of phthalates exposure when high fruit consumption and personal care products use are linked to higher phthalate metabolite contents in the urine. However, this topic deserves more research.

hero.3469454

Nassan, FL; Coull, BA; Skakkebaek, NE; Williams, MA; Dadd, R; Mínguez-Alarcón, L; Krawetz, SA; Hait, EJ; Korzenik, JR; Moss, AC; Ford, JB; Hauser, R. (2016). A crossover-crossback prospective study of dibutyl-phthalate exposure from mesalamine medications and semen quality in men with inflammatory bowel disease. Environ Int 95: 120-130. http://dx.doi.org/10.1016/j.envint.2016.08.006.

BACKGROUND: Phthalates are widely used chemicals with ubiquitous exposure. Dibutyl-phthalate (DBP), a male reproductive toxicant in animals, is understudied in humans. Some mesalamine medications used to treat inflammatory bowel disease (IBD) have DBP in their coating, whereas other mesalamine formulations do not.

OBJECTIVES: Taking advantage of

differences in mesalamine formulations, we investigated whether high-DBP exposure from mesalamine medications was associated with decreased semen parameters.

METHODS: 73 men with IBD taking mesalamine participated in a crossover-crossback prospective study. Men taking non-DBP containing mesalamine at baseline i.e., background exposure, crossed-over for four months to high-DBP mesalamine and then crossed-back for four months to their non-DBP mesalamine (B1HB2-arm;Background1-High-Background2) and vice versa for men taking high-DBP mesalamine at baseline (H1BH2-arm;High1-Background-High2). Men provided up to six semen samples (2: baseline, 2: crossover and 2: crossback).

RESULTS: We estimated crossover, crossback and carryover effects using linear mixed models adjusted for abstinence time, age, season and duration on high-DBP mesalamine at baseline. Semen parameters in B1HB2-arm (26 men, 133 samples) decreased after high-DBP mesalamine exposure (crossover versus baseline), especially motility parameters, and continued to decrease further even after crossback to non-DBP mesalamine (crossback versus crossover). The cumulative carryover effect of high-DBP (crossback versus baseline) was a decrease of % total sperm motility by 7.61(CI:-13.1, -2.15), % progressive sperm motility by 4.23(CI:-8.05, -0.4) and motile sperm count by 26.0% (CI:-46.2%, 1.7%). However, H1BH2-arm (47 men, 199 samples) had no significant change during crossover or crossback.

CONCLUSIONS: Men newly exposed to high-DBP mesalamine for four months had a cumulative reduction in several semen parameters, primarily sperm motility, that was more pronounced and statistically significant even after exposure ended for four months.

hero.3070957

Ni, J; Zhang, Z; Luo, X; Xiao, L; Wang, N. (2015). Plasticizer DBP Activates NLRP3 Inflammasome through the P2X7 Receptor in HepG2 and L02 Cells. J Biochem Mol Toxicol 30: 178-185. http://dx.doi.org/10.1002/jbt.21776.

Ditubyl phthalate (DBP), one of the most widely used plasticizers, can migrate out to contaminate our bodies and environment. A number of studies have showed that DBP is closely related to liver pathological changes and diseases. Inflammasomes are multiprotein complexes composed of procaspase and pattern recognition receptors such as Nucleotide oligomerization domain (NOD) like receptor family, pyrin domain containing 3 (NLRP3). Activation of NLRP3 inflammasome is implicated in the pathogeneses of liver damage. The aim of this study was to determine the effects of DBP on NLRP3 inflammasome. We found that DBP triggered the activation of NLRP3 inflammasome in hepatocyte cell lines. By using Ca-074-Me, N-acetylcysteine and KN-62, we observed that the P2X7 receptor participated in the DBP-induced activation of NLRP3 inflammasome. DBP could also trigger the ATP release. In conclusion, we demonstrated that DBP is one of the activator of NLRP3 inflammasome and may play an important role in liver damage.

hero.3469551

Nicole, W. (2016). Phthalates and Childhood Body Fat: Study Finds No Evidence of Obesogenicity [Comment]. Environ Health Perspect 124: A78. http://dx.doi.org/10.1289/ehp.124-A78.

hero.3479498 REVIEW

NTP (National Toxicology Program). (2000). Center for the evaluation of risks to human reproduction: NTP-CERHR expert panel report on di-n-butyl phthalate. Gov Rep Announce Index.

The National Toxicology Program (NTP) and the National Institute of Environmental Health Sciences established the NTP Center for the Evaluation of Risks to Human Reproduction (CERHR) in June, 1998. The purpose of the Center is to provide timely, unbiased, scientifically sound evaluations of human and experimental evidence for adverse effects on reproduction, including development, caused by agents to which humans may be exposed. The following seven phthalate esters were selected for the initial evaluation by the Center: butyl benzyl phthalate, di(2-ethylhexyl) phthalate, di-isodecyl phthalate, di-isononyl phthalate, di-n-butyl phthalate, di-nhexyl phthalate, and di-n-octyl phthalate. Phthalate esters are used as plasticizers in a wide range of polyvinyl chloride-based consumer products. These chemicals were selected for the initial evaluation by the CERHR based on their high production volume, extent of human exposures, use in children's products, published evidence of reproductive or developmental toxicity, and public concern.

hero.3469482

Oca, ML; Rubio, L; Sarabia, LA; Ortiz, MC. (2016). Dealing with the ubiquity of phthalates in the laboratory when determining plasticizers by gas chromatography/mass spectrometry and PARAFAC. J Chromatogr A 1464:

124-140. http://dx.doi.org/10.1016/j.chroma.2016.07.074.
Determining plasticizers and other additives migrated from plastic materials becomes a hard task when these substances are already present in the laboratory environment. This work dealt with this drawback in the multiresidue determination of four plasticizers (2,6-di-tert-butyl-4-methyl-phenol (BHT), diisobutyl phthalate (DiBP), bis(2-ethylhexyl) adipate (DEHA) and diisononyl phthalate (DiNP)) and a UV stabilizer (benzophenone (BP)) by gas chromatography/mass spectrometry (GC/MS) using DiBP-d4 as internal standard. The ubiquity of DiBP by a non-constant leaching process in the laboratory was detected, which could not guarantee the achievement of a trustworthy quantification. To handle this, the assessment of the level of DiBP in solvent blanks having fixed the probabilities of false non-compliance (α) and false compliance (β) at 0.01 was performed. On the other hand, another special case was that of DiNP, in whose chromatogram finger peaks appear because of an array of possible C9 isomers. PARAFAC, used for the identification and quantification of all the substances, is a useful chemometric tool that enabled a more reliable determination of this analyte since no peak areas were considered but chromatographic and spectral loadings. Since phthalates may migrate from rubber latex items, an evaluation of the existence of matrix effects on the determination of the five analytes was conducted prior to an extraction with hexane from a dummy for infants. As matrix effects were present, the quantification of the compounds under study was performed following the standard addition method using PARAFAC sample loadings as response variable. As a result, the presence of BHT was confirmed, being its concentration equal to 37.87μgL(-1). Calibrations based on PARAFAC yielded the following values for the decision limit (CCα): 1.16μgL(-1) for BHT, 1.34μgL(-1) for BP, 1.84μgL(-1) for DEHA and 51.42μgL(-1) for DiNP(for α=0.05 and two replicates).

hero.3469544

Ortega-García, JA; Olano-Soler, HA; Martínez-Álvarez, A; Campillo-López, F; Gomariz-Peñalver, V; Mendiola-Olivares, J; Iglesias-Gómez, C; Escribano-Muñoz, A. (2016). Breastfeeding Duration and Anogenital Distance in 2-Year-Old Infants. Breastfeed Med 11: 350-355. http://dx.doi.org/10.1089/bfm.2016.0034.
BACKGROUND: The anogenital distance (AGD) is an anthropometric marker determined by exposures to androgens in utero and throughout the first few months of life. Early exposures to endocrine-disrupting chemicals such as phthalates have been significantly associated with shortened AGD in boys. Limited studies have explored phthalate concentrations in breast milk and infant formula.

OBJECTIVE: To explore the associations between breastfeeding duration and AGD measures in infants.

MATERIALS AND METHODS: MALAMA (Medio Ambiente y Lactancia Materna) is a follow-up study of 430 mother-child pairs, from birth to 2 years, from two population-based cohorts in Murcia, Spain. Data were collected through medical visits and telephone surveys from birth to 2 years of age. World Health Organization breastfeeding definitions were used. AGD measurements were assessed in a subsample of 71 boys and 49 girls at the 2-year visit. Descriptive analyses, Pearson correlations, and linear regressions were calculated between AGD and breastfeeding duration.

RESULTS: Duration of all types of breastfeeding, especially full breastfeeding (FB), is correlated with AGD measures in boys (p < 0.05). AGDAS (anoscrotal distance) and AGDAP (anopenile distance) were positively associated with FB (β = 0.004, 95%CI: 0.001-0.007 and β = 0.003, 95%CI: 0.000-0.007, respectively).

CONCLUSIONS: A positive correlation between AGD in male infants and the duration of breastfeeding is reported. Inversely, early introduction of infant formula could lead to the reduction of AGD in boys.

hero.3455857

Ouyang, X; Weiss, JM; de Boer, J; Lamoree, MH; Leonards, PE. (2017). Non-target analysis of household dust and laundry dryer lint using comprehensive two-dimensional liquid chromatography coupled with time-of-flight mass spectrometry. Chemosphere 166: 431-437. http://dx.doi.org/10.1016/j.chemosphere.2016.09.107.
Household dust and laundry dryer lint are important indoor environmental matrices that may have notable health effects on humans due to chronic exposure. However, due to the sample complexity the studies conducted on these sample matrices until now were almost exclusively on the basis of target analysis. In this study, comprehensive two-dimensional liquid chromatography coupled with time-of-flight mass spectrometry (LCLC-ToF MS) was applied, to enable non-target analysis of household dust as well as laundry dryer lint for the first time. The higher peak capacity and good orthogonality of LCLC, together with reduced ion suppression in the MS enabled rapid identification of environmental contaminants in these complex

sample matrices. A number of environmental contaminants were tentatively identified based on their accurate masses and isotopic patterns, including plasticizers, flame retardants, pesticides, drug metabolites, etc. The identity of seven compounds: tris(2-butoxyethyl) phosphate, tris(2-chloropropyl) phosphate, n-benzyl butyl phthalate, dibutyl phthalate, tributyl phosphate, triethyl phosphate and N, N-diethyl-meta-toluamide was confirmed using two-dimensional retention alignment and their concentrations in the samples were semi-quantitatively determined.

hero.3479509

Ozaki, H; Sugihara, K; Watanabe, Y; Ohta, S; Kitamura, S. (2016). Cytochrome P450-inhibitory activity of parabens and phthalates used in consumer products. J Toxicol Sci 41: 551-560.

The in vitro cytochrome P450 (CYP)-inhibitory effects of 11 parabens and 7 phthalates used in consumer products, as well as their hydrolytic metabolites, were investigated, using rat liver microsomes as an enzyme source. The effects on individual CYP isozymes were evaluated by assaying inhibition of activities towards specific substrates, i.e., ethoxyresorufin O-dealkylase (EROD), methoxyresorufin O-dealkylase (MROD), pentoxyresorufin O-dealkylase (PROD), 7-benzyloxy-4-trifluoromethylcoumarin dealkylase (BFCD), 7-methoxy-4-trifiuoromethylcoumarin dealkylase (MFCD) and 7-ethoxy-4-trifluoromethylcoumarin dealkylase (EFCD) activities. These activities were dose-dependently inhibited, most potently by medium-side-chain parabens (C6-9) and phthalates (C4-6), and less potently by shorter and longer-side-chain esters. The hydrolytic product of parabens, 4-hydroxybenzoic acid, was not inhibitory, while those of phthalates, phthalic acid monoesters, showed lower inhibitory activity than the parent phthalates. Parabens showed relatively potent inhibition of MFCD activity, considered to be mainly due to CYP2C, and phthalates showed relatively potent inhibition of PROD activity, considered to be mainly due to CYP2B.

hero.3350210

Pan, Y; Jing, J; Yeung, LW; Sheng, N; Zhang, H; Yao, B; Dai, J. (2016). Associations of urinary 5-methyl-2'-deoxycytidine and 5-hydroxymethyl-2'-deoxycytidine with phthalate exposure and semen quality in 562 Chinese adult men. Environ Int 94: 583-590. http://dx.doi.org/10.1016/j.envint.2016.06.020.

5-methyl-2'-deoxycytidine (5mdC) and 5-hydroxymethyl-2'-deoxycytidine (5hmdC), products of DNA methylation and hydroxymethylation processes, have been detected previously in human urine, but their associations with environmental chemicals or healthy outcomes are unclear. The present investigation explored the associations between urinary 5mdC and 5hmdC with phthalate exposure and semen quality. We assessed semen parameters including sperm concentration, motility, and morphology, before measuring urinary 5mdC, 5hmdC and 13 phthalate metabolites among 562 subfertile men from Nanjing, China. Urinary 5mdC and 5hmdC were positively associated with the levels of low molecular weight phthalate metabolites (Low-MWP), high molecular weight phthalate metabolites (High-MWP), and the sum of all phthalate metabolites (ΣPAEs), respectively. Urinary 5mdC was associated with below-reference sperm concentration (odds ratios for increasing quartiles=1.0, 2.2, 3.0, 2.0; p for trend =0.02), sperm motility (1.0, 1.1, 1.9, 1.3; p for trend =0.05), and sperm morphology (1.0, 1.4, 2.3, 1.5; p for trend =0.05). Sperm concentration was associated with the highest quartile of urinary 5hmdC [odds ratio=1.9 (95% CI: 1.1, 3.6)]. Our findings showed significant associations between urinary 5mdC and 5hmdC with phthalate metabolites and semen parameters, which suggested urinary 5mdC and 5hmdC may be promising biomarkers in future epidemiological studies.

hero.3479533

Pariatamby, A; Kee, YL. (2016). Persistent organic pollutants management and remediation. Procedia Environ Sci 31: 842-848. http://dx.doi.org/10.1016/j.proenv.2016.02.093.

Persistent organic pollutants (POPs) are toxic chemicals that originate from man-made sources associated with the production, use, and disposal of certain organic chemicals. Many of the chemicals were produced commercially for pest and disease control, crop production and industrial use. Some of the POPs such as pesticides and polychlorinated biphenyls (PCBs) are intentionally produced, while others such as dioxins and furans are unintentional by-products of industrial processes or result from the combustion of organic chemicals. Over the last six decades, the unsustainable management of chemicals through their life cycles has resulted in widespread and massive contamination of the environment, biota and humans with POPs and other persistent toxic substances. Many techniques had been used for treating POPs. However, these

techniques did not prove to be highly efficient due to the high operational costs involved. Recent studies found that, Guar gum and Xanthan gum are highly recommended as an option for treating POPs, because it is a biodegradable biopolymer, non-toxic, involved low treatment cost, easily available and is produced in abundance. (C) 2016 The Authors. Published by Elsevier B.V.

hero.3469477

Percy, Z; Xu, Y; Sucharew, H; Khoury, JC; Calafat, AM; Braun, JM; Lanphear, BP; Chen, A; Yolton, K. (2016). Gestational exposure to phthalates and gender-related play behaviors in 8-year-old children: an observational study. Environ Health 15: 87. http://dx.doi.org/10.1186/s12940-016-0171-7.

BACKGROUND: Phthalates, used in a variety of consumer products, are a group of chemicals that are ubiquitous in the environment, and their metabolites are detectable in most humans. Some phthalates have anti-androgenic properties; a prior study reported an association between gestational exposure to phthalates and reduced masculine behaviors in preschool boys.

METHODS: Concentrations of 9 phthalate metabolites were measured in urine collected at 16 and 26weeks' gestation from pregnant women enrolled in the HOME Study, a prospective pregnancy and birth cohort. Measures of gender-related play were collected at 8years of age, including the Gender Identity Questionnaire (GIQ) completed by mothers, and the Playmate and Play Style Preferences Structured Interview (PPPSI) completed by children. We examined these measures as continuous variables using both bivariate and multivariable approaches with adjustment for covariates. Additional analyses included logistic regression of GIQ and PPPSI scores dichotomized by sex at the lower 25th percentile, indicating the least typical behavior.

RESULTS: Mothers' phthalate metabolite concentrations during pregnancy were similar to the reported national average among US women. All children scored within a typical range on both measures of gender-related play behavior. No statistically significant associations were found between averaged maternal phthalate metabolite concentrations and continuous PPPSI scores or any GIQ scores. For the dichotomized PPPSI; higher maternal monoethyl phthalate (MEP) concentrations were associated with more typical play behaviors for females (OR = 0.70, CI = 0.51-0.97). In contrast, higher maternal mono-isobutyl phthalate (MiBP) concentrations were associated with higher odds of membership in the least typical play behaviors group for males (OR = 1.69, CI = 1.00-2.86).

CONCLUSIONS: In this sample of typically developing children, higher maternal urinary MEP concentrations during pregnancy were associated with more typical gender-related play behaviors in both males and females, and increased urinary MiBP concentrations were associated with less masculine gender-related play behaviors in males.

hero.3479527

Perera, F; Nolte, EL; Wang, Y; Margolis, AE; Calafat, AM; Wang, S; Garcia, W; Hoepner, LA; Peterson, BS; Rauh, V; Herbstman, J. (2016). Bisphenol A exposure and symptoms of anxiety and depression among inner city children at 10-12 years of age. Environ Res 151: 195-202. http://dx.doi.org/10.1016/j.envres.2016.07.028.

BACKGROUND: Experimental and epidemiological studies suggest that gestational exposure to Bisphenol A (BPA), an ubiquitous endocrine disrupting chemical, may lead to neurobehavioral problems in childhood; however, not all results have been consistent. We previously reported a positive association between prenatal BPA exposure and symptoms of anxiety/depression reported by the mother at child age 7-9 years in boys, but not girls.

OBJECTIVES: Here, in the same birth cohort, we investigated the association of prenatal BPA exposure with symptoms of depression and anxiety self-reported by the 10-12 year olds, hypothesizing that we would observe sex-specific differences in anxiety and depressive symptoms.

METHODS: African-American and Dominican women living in Northern Manhattan and their children were followed from mother's pregnancy through children's age 10-12 years. BPA was quantified in maternal urine collected during the third trimester of pregnancy and in child urine collected at ages 3 and 5 years. Children were evaluated using the Revised Children's Manifest Anxiety Scale (RCMAS) and Children's Depression Rating Scale (CDRS). We compared the children in the highest tertile of BPA concentration to those in the lower two tertiles. Associations between behavior and prenatal (maternal) BPA concentration or postnatal (child) BPA concentration were assessed in regression models stratified by sex.

RESULTS: Significant positive associations between prenatal BPA and symptoms of depression and anxiety were observed among boys. Postnatal BPA exposure was not significantly associated with outcomes. There was substantial co-occurrence

of anxiety and depressive symptoms in this sample.

CONCLUSION: These results provide evidence that prenatal BPA exposure is associated with more symptoms of anxiety and depression in boys but not in girls at age 10-12 years.

hero.3469255

Pérez-Albaladejo, E; Fernandes, D; Lacorte, S; Porte, C. (2017). Comparative toxicity, oxidative stress and endocrine disruption potential of plasticizers in JEG-3 human placental cells. Toxicol in Vitro 38: 41-48. http://dx.doi.org/10.1016/j.tiv.2016.11.003.

Plasticizers are suspected to be toxic and/or to modulate or disrupt the endocrine system of humans and to cross the placental barrier, being embryonic and fetal development a particularly vulnerable period. This work investigates the comparative toxicity and ability to interfere with the synthesis of steroids and to generate reactive oxygen species (ROS) of a selected number of plasticizers, including bisphenol A (BPA), nonyl- (NP) and octylphenol (OP), benzyl butyl phthalate (BBP), dibutyl phthalate (DBP), di(2-ethylhexyl)phthalate (DEHP) and dimethyl phthalate (DMP), in the human placenta JEG-3 cells. Moreover, the bioavailability of chemicals in culture medium has been investigated. After 24h exposure, OP and NP showed the highest cytotoxicity (EC50: 36-40μM) followed by BPA (138-219μM), whereas no significant toxicity was observed for phthalates. Notwithstanding, BBP and DBP significantly decreased P450 aromatase activity (experimental IC50: 14-15μM), while NP and OP (20μM) increased the activity. Overall, this study evidences the differential toxicity and ability to modulate placental aromatase activity of some of the compounds nowadays used as plasticizers, and highlights the need of an accurate determination of the bioavailability of chemicals to improve the sensitivity of in-vitro tests.

hero.3469422

Petrovičová, I; Kolena, B; Šidlovská, M; Pilka, T; Wimmerová, S; Trnovec, T. (2016). Occupational exposure to phthalates in relation to gender, consumer practices and body composition. Environ Sci Pollut Res 23: 24125-24134. http://dx.doi.org/10.1007/s11356-016-7394-6.

The aim of our work was to find associations between urinary phthalate metabolite concentrations and occupation, consumer practices and body composition. We divided our cohort (n=129) into occupationally exposed subjects, community service workers (group A; n=45) and workers from plastic industry (group B; n=35) and group of general population (control group C, n=49). To estimate levels of five phthalate metabolites, we used high-performance liquid chromatography and tandem mass spectrometry analysis. We found in plastic industry workers compared to community service workers and subjects of the control group significantly higher urinary concentration mono (2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono (2-ethyl-5-oxohexyl) phthalate (MEOHP), mono (2-etylhexyl) phthalate (MEHP), sum di-(2-ethyl-5-oxohexyl) phthalate (DEHP), mono-iso-butyl phthalate (MiBP) and mono-n-butyl phthalate (MnBP). We identified by multivariate analysis of covariance inverse relationship between MEHP and body parameters as waist-to-height ratio, body mass index, waist-to-hip ratio, hip circumference and waist circumference among females, whereas in males, no significant association was found. Results of our study show, despite of variability in terms of occupational exposure to phthalates, that plastic manufactory represents a higher occupational risk in comparison with waste management. The differences in anthropometric parameters between the two occupationally exposed groups and the general population are suggesting a detrimental effect of occupational exposure on body weight homeostasis.

hero.3469443 REVIEW

Philips, EM; Jaddoe, VW; Trasande, L. (2016). Effects of early exposure to phthalates and bisphenols on cardiometabolic outcomes in pregnancy and childhood [Review]. Reprod Toxicol. http://dx.doi.org/10.1016/j.reprotox.2016.08.015.

Pregnant women are exposed to various chemicals, including endocrine-disrupting chemicals (EDCs) such as phthalates and bisphenols. Increasing evidence suggests that early life exposures to phthalates and bisphenols may contribute to cardiometabolic risks. The aim of this narrative review was to summarize current knowledge of the effects of fetal and childhood exposure to phthalates and bisphenols on child growth and child cardiometabolic outcomes and the effects on maternal outcomes. In total, 54 studies were identified and included. The majority of studies found effects of phthalates and bisphenols on maternal, child growth, and cardiometabolic outcomes. Currently results suggest that early life exposure to phthalates and

bisphenols may have a substantial influence on perinatal and postnatal cardiometabolic programming. In a large part of the investigated outcomes studies show contradictory results. However, the majority of the existing evidence is based on non-cohort studies with single samples neglecting time-variant effects and complicating conclusions regarding causal inference. More studies are needed investigating the mechanisms and its potential interactions.

hero.3469565

Phuong, C; Maibach, HI. (2016). Recent knowledge: Concepts of dermal absorption in relation to skin decontamination [Review]. J Appl Toxicol 36: 5-9. http://dx.doi.org/10.1002/jat.3222.

Skin decontamination is an important step mitigating percutaneous absorption through the stratum corneum (SC), which is also a highly complex process. Thus, understanding diffusion mechanisms and measuring dermal absorption rates are critical to protect humans from toxic exposures. Here, highly varied literature is placed in a biological and clinical perspective in regards to decontamination. Literature from PubMed and Surge Laboratory library files were searched and reviewed for relevance. Recent data have shown multiple layers of SC structural heterogeneity, which results in unique substance partitioning characteristics across the membrane. As such, attempts to model and understand this behavior in alternative in vitro membranes prove difficult. More synthetic and natural membranes are being explored as models for in vivo behavior. In addition, commonly accepted decontamination methods are undergoing risk assessment. These recent and varied literature findings update available knowledge regarding skin decontamination and its challenges, with a focus on dermal absorption.

hero.3469532

Polańska, K; Ligocka, D; Sobala, W; Hanke, W. (2016). Effect of environmental phthalate exposure on pregnancy duration and birth outcomes. Int J Occup Med Environ Health 29: 683-697. http://dx.doi.org/10.13075/ijomeh.1896.00691.

OBJECTIVES: The objective of this study was to evaluate the impact of phthalate exposure on pregnancy duration and birth outcomes based on the Polish Mother and Child Cohort (REPRO_PL).

MATERIAL AND METHODS: Phthalate exposure was determined by measuring 11 phthalate metabolites (mono-ethyl phthalate (MEP), mono-iso-butyl phthalate (MiBP), mono-n-butyl phthalate (MnBP), 3OH-mono-n-butyl phthalate (OH-MnBP), mono-benzyl phthalate (MBzP), mono (2-ethylhexyl) phthalate (MEHP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), mono-hydroxy-iso-nonyl phthalate (MHiNP), mono-oxo-iso-nonyl phthalate (MOiNP), and mono-n-octyl phthalate (MOP)) in the urine collected from 165 mothers during the third trimester of pregnancy by high performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS). The following measures at birth were considered: gestational age, birth weight, length as well as head and chest circumference.

RESULTS: Pregnancy duration was inversely associated with natural log concentrations (μg/g creatinine) of MEP (standardized regression coefficient (β) = -0.2, p = 0.04) after adjustment for a variety of confounders. Significant impact of MOiNP on head circumference (β = -0.1, p = 0.05) was also observed.

CONCLUSIONS: The study findings add further support to the hypothesis that phthalate exposure may be associated with shorter pregnancy duration and a decreased head circumference, and underscore importance of public health interventions to reduce that exposure.

hero.3466558

Polidoro, BA; Comeros-Raynal, MT; Cahill, T; Clement, C. (2017). Land-based sources of marine pollution: Pesticides, PAHs and phthalates in coastal stream water, and heavy metals in coastal stream sediments in American Samoa. Mar Pollut Bull. http://dx.doi.org/10.1016/j.marpolbul.2016.12.058.

The island nations and territories of the South Pacific are facing a number of pressing environmental concerns, including solid waste management and coastal pollution. Here we provide baseline information on the presence and concentration of heavy metals and selected organic contaminants (pesticides, PAHs, phthalates) in 7 coastal streams and in surface waters adjacent to the Futiga landfill in American Samoa. All sampled stream sediments contained high concentrations of lead, and some of mercury. Several coastal stream waters showed relatively high concentrations of diethyl phthalate and of organophosphate pesticides, above chronic toxicity values for fish and other aquatic organisms. Parathion, which has been

banned by the US Environmental Protection Agency since 2006, was detected in several stream sites. Increased monitoring and initiatives to limit non-point source land-based pollution will greatly improve the state of freshwater and coastal resources, as well as reduce risks to human health in American Samoa.

hero.3479528

Pollack, AZ; Perkins, NJ; Sjaarda, L; Mumford, SL; Kannan, K; Philippat, C; Wactawski-Wende, J; Schisterman, EF. (2016). Variability and exposure classification of urinary phenol and paraben metabolite concentrations in reproductive-aged women. Environ Res 151: 513-520. http://dx.doi.org/10.1016/j.envres.2016.08.016. BACKGROUND: Human exposure to phenols and parabens is widespread. Within-person variability of urinary concentrations in healthy women is not well characterized.

OBJECTIVES: To characterize the variability of urinary phenol and paraben concentrations across two months and evaluate the ability of a single spot urine sample to characterize exposure.

METHODS: 143 women provided 509 spot urine samples collected across two months of study (3-5 samples/woman). We measured urinary concentrations of 8 phenols: bisphenol A (BPA), benzophenone-3 (BP-3), benzophenone-1 (BP-1), 2,4-dichlorophenol (2,4-DCP), 2,5-dichlorophenol (2,5-DCP), 2,4,5-trichlorophenol (2,4,5-TCP), 2,4,6-trichlorophenol (2,4,6-TCP), triclosan (TCS); and 8 parabens and their metabolites (benzyl (BzP), butyl (BuP), ethyl (EtP), heptyl (HeP), methyl (MeP), propyl (PrP), 4-hydroxybenzoic acid (4-HB), 3,4-dihydroxybenzoic acid (3,4-DHB)). Biomarker variability was characterized using the intraclass correlation coefficient (ICC) and surrogate category analyses were conducted.

RESULTS: ICCs ranged from very low for BPA (0.04) to moderate for BP-3, BP-1, TCS, BzP, and MeP (0.66, 0.58, 0.55, 0.54, and 0.62, respectively). Surrogate analyses suggested that BP-1, BP-3, TCS, 2,4-DCP, BuP, and PrP may be characterized by a single spot sample (sensitivity range 0.76-0.86) but that additional samples were necessary for BPA, HeP, 4-HB, and 3,4-DHB (sensitivity range 0.47-0.61).

CONCLUSIONS: Urinary phenol and paraben metabolite concentrations were variable across two months in healthy women but the degree of reliability differed by the specific biomarker. A small number of samples may sufficiently characterize typical concentrations for BP-3, BP-1, TCS, BuP, and PrP; but additional biospecimens may be necessary to characterize exposure for other compounds, including BPA.

hero.3466586

Preciados, M; Yoo, C; Roy, D. (2016). Estrogenic Endocrine Disrupting Chemicals Influencing NRF1 Regulated Gene Networks in the Development of Complex Human Brain Diseases [Review]. Int J Mol Sci 17. http://dx.doi.org/10.3390/ijms17122086.

During the development of an individual from a single cell to prenatal stages to adolescence to adulthood and through the complete life span, humans are exposed to countless environmental and stochastic factors, including estrogenic endocrine disrupting chemicals. Brain cells and neural circuits are likely to be influenced by estrogenic endocrine disruptors (EEDs) because they strongly dependent on estrogens. In this review, we discuss both environmental, epidemiological, and experimental evidence on brain health with exposure to oral contraceptives, hormonal therapy, and EEDs such as bisphenol-A (BPA), polychlorinated biphenyls (PCBs), phthalates, and metalloestrogens, such as, arsenic, cadmium, and manganese. Also we discuss the brain health effects associated from exposure to EEDs including the promotion of neurodegeneration, protection against neurodegeneration, and involvement in various neurological deficits; changes in rearing behavior, locomotion, anxiety, learning difficulties, memory issues, and neuronal abnormalities. The effects of EEDs on the brain are varied during the entire life span and far-reaching with many different mechanisms. To understand endocrine disrupting chemicals mechanisms, we use bioinformatics, molecular, and epidemiologic approaches. Through those approaches, we learn how the effects of EEDs on the brain go beyond known mechanism to disrupt the circulatory and neural estrogen function and estrogen-mediated signaling. Effects on EEDs-modified estrogen and nuclear respiratory factor 1 (NRF1) signaling genes with exposure to natural estrogen, pharmacological estrogen-ethinyl estradiol, PCBs, phthalates, BPA, and metalloestrogens are presented here. Bioinformatics analysis of gene-EEDs interactions and brain disease associations identified hundreds of genes that were altered by exposure to estrogen, phthalate, PCBs, BPA or metalloestrogens. Many genes modified by EEDs are common targets of both 17 β-estradiol (E2) and NRF1. Some of these genes are involved with brain diseases, such as Alzheimer's Disease (AD), Parkinson's Disease, Huntington's Disease, Amyotrophic Lateral Sclerosis, Autism Spectrum Disorder, and Brain Neoplasms. For

example, the search of enriched pathways showed that top ten E2 interacting genes in AD-APOE, APP, ATP5A1, CALM1, CASP3, GSK3B, IL1B, MAPT, PSEN2 and TNF-underlie the enrichment of the Kyoto Encyclopedia of Genes and Genomes (KEGG) AD pathway. With AD, the six E2-responsive genes are NRF1 target genes: APBB2, DPYSL2, EIF2S1, ENO1, MAPT, and PAXIP1. These genes are also responsive to the following EEDs: ethinyl estradiol (APBB2, DPYSL2, EIF2S1, ENO1, MAPT, and PAXIP1), BPA (APBB2, EIF2S1, ENO1, MAPT, and PAXIP1), dibutyl phthalate (DPYSL2, EIF2S1, and ENO1), diethylhexyl phthalate (DPYSL2 and MAPT). To validate findings from Comparative Toxicogenomics Database (CTD) curated data, we used Bayesian network (BN) analysis on microarray data of AD patients. We observed that both gender and NRF1 were associated with AD. The female NRF1 gene network is completely different from male human AD patients. AD-associated NRF1 target genes-APLP1, APP, GRIN1, GRIN2B, MAPT, PSEN2, PEN2, and IDE-are also regulated by E2. NRF1 regulates targets genes with diverse functions, including cell growth, apoptosis/autophagy, mitochondrial biogenesis, genomic instability, neurogenesis, neuroplasticity, synaptogenesis, and senescence. By activating or repressing the genes involved in cell proliferation, growth suppression, DNA damage/repair, apoptosis/autophagy, angiogenesis, estrogen signaling, neurogenesis, synaptogenesis, and senescence, and inducing a wide range of DNA damage, genomic instability and DNA methylation and transcriptional repression, NRF1 may act as a major regulator of EEDs-induced brain health deficits. In summary, estrogenic endocrine disrupting chemicals-modified genes in brain health deficits are part of both estrogen and NRF1 signaling pathways. Our findings suggest that in addition to estrogen signaling, EEDs influencing NRF1 regulated communities of genes acro s genomic and epigenomic multiple networks may contribute in the development of complex chronic human brain health disorders.

hero.3479506

Przybylinska, PA; Wyszkowski, M. (2016). ENVIRONMENTAL CONTAMINATION WITH PHTHALATES AND ITS IMPACT ON LIVING ORGANISMS. 23: 347-356. http://dx.doi.org/10.1515/eces-2016-0024.

The relevant literature was reviewed to identify phthalate sources in the environment and problems resulting from phthalate contamination of soil and water. Phthalate properties responsible for their toxicity for living organisms were identified, and the effects of phthalates on humans and animals were described. Special emphasis was placed on the effects of exposure to phthalates on human health. Phthalates are readily released into the environment and create a risk of exposure for humans and other living organisms. They are characterized by reproductive toxicity in humans and animals, they can cause infertility and reproductive problems in males. Phthalates are more toxic in young children, which are much more susceptible to phthalate exposure, including fetal life. Phthalates are used in numerous industries, and they are very difficult to eliminate from our daily surroundings.

hero.3479503

Rathinamoorthy, R; Thilagavathi, G. (2016). GC-MS Analysis of Worn Textile for Odour Formation. Fibers and Polymers 17: 917-924. http://dx.doi.org/10.1007/s12221-016-5891-3.

Odour formation in the textile is a serious and embarrassing problem for an individual. The axilla born bacterial species are noted as the main reason for odour formation in axilla. In this research an attempt has been made to identify the odour generating compounds on the textile material after wear trial using gas chromatography and mass spectrum (GC-MS). The result indicates that the worn textile material consisted steroidal fractions of 5 alpha-androst-16-ene-3-one and cholesterol, the major odour forming source from axilla. The results also identified the other important odour forming fatty acids and alcohols like lauric acids, diethyl esters of 1,2-benzenedicarboxylic acid, methyl esters of tetradecanoic acid, 3-methylhexanoic acid, Tetradecanol and acetic acid in axilla worn textile. These components were the derivatives of axilla specific odourous components like phthalic acid, myristic acid, isobutric acid and alcohols. The effect of Terminalia chebula extract finish on the odour formation also analysed and the results shows a considerable reduction in odour causing short chain volatile fatty acids (VFAs) in the worn textile compare to the untreated textile. The analysis also identified more amounts of active components of Terminalia chebula on the fabric surface instead of the odourous components from axilla.

hero.3469427

Rendel, F; Alfredsson, CF; Bornehag, CG; Sundström, BE; Nånberg, E. (2016). Effects of Di-Isononyl Phthalate on Neuropeptide Y Expression in Differentiating Human Neuronal Cells. Basic & Clinical Pharmacology &

Toxicology Online Pharmacology Online. http://dx.doi.org/10.1111/bcpt.12670.
Neuropeptide Y (NPY) is an abundant neuropeptide in the mammalian brain important for behavioural consequences of stress and energy metabolism. We have addressed possible effects of the phthalate DiNP on NPY expression in human SH-SY5Y cells, a neuronal in vitro differentiation model. Pico- to nanomolar doses of DiNP and its metabolite MiNP resulted in decreased NPY mRNA and peptide expression in retinoid-differentiated cells. Thus, dys-regulated NPY may be an adverse outcome for exposure to low doses of DiNP in human beings. This article is protected by copyright. All rights reserved.

hero.3469390

Rich, AL; Phipps, LM; Tiwari, S; Rudraraju, H; Dokpesi, PO. (2016). The Increasing Prevalence in Intersex Variation from Toxicological Dysregulation in Fetal Reproductive Tissue Differentiation and Development by Endocrine-Disrupting Chemicals [Review]. Environ Health Insights 10: 163-171. http://dx.doi.org/10.4137/EHI.S39825.
An increasing number of children are born with intersex variation (IV; ambiguous genitalia/hermaphrodite, pseudohermaphroditism, etc.). Evidence shows that endocrine-disrupting chemicals (EDCs) in the environment can cause reproductive variation through dysregulation of normal reproductive tissue differentiation, growth, and maturation if the fetus is exposed to EDCs during critical developmental times in utero. Animal studies support fish and reptile embryos exhibited IV and sex reversal when exposed to EDCs. Occupational studies verified higher prevalence of offspring with IV in chemically exposed workers (male and female). Chemicals associated with endocrine-disrupting ability in humans include organochlorine pesticides, poly-chlorinated biphenyls, bisphenol A, phthalates, dioxins, and furans. Intersex individuals may have concurrent physical disorders requiring lifelong medical intervention and experience gender dysphoria. An urgent need exists to determine which chemicals possess the greatest risk for IV and the mechanisms by which these chemicals are capable of interfering with normal physiological development in children.

hero.3350315

Rojas, D; Jurado-Sánchez, B; Escarpa, A. (2016). "Shoot and Sense" Janus Micromotors-Based Strategy for the Simultaneous Degradation and Detection of Persistent Organic Pollutants in Food and Biological Samples. Anal Chem 88: 4153-4160. http://dx.doi.org/10.1021/acs.analchem.6b00574.
A novel Janus micromotor-based strategy for the direct determination of diphenyl phthalate (DPP) in food and biological samples is presented. Mg/Au Janus micromotors are employed as novel analytical platforms for the degradation of the non-electroactive DPP into phenol, which is directly measured by difference pulse voltammetry on disposable screen-printed electrodes. The self-movement of the micromotors along the samples result in the generation of hydrogen microbubbles and hydroxyl ions for DPP degradation. The increased fluid transport improves dramatically the analytical signal, increasing the sensitivity while lowering the detection potential. The method has been successfully applied to the direct analysis of DPP in selected food and biological samples, without any sample treatment and avoiding any potential contamination from laboratory equipment. The developed approach is fast (5 min) and accurate with recoveries of 100%. In addition, efficient propulsion of multiple Mg/Au micromotors in complex samples has also been demonstrated. The advantages of the micromotors-assisted technology, i.e., disposability, portability, and the possibility to carry out multiple analysis simultaneously, hold considerable promise for its application in food and biological control in analytical applications with high significance.

hero.3466566

Rosofsky, A; Janulewicz, P; Thayer, KA; Mcclean, M; Wise, LA; Calafat, AM; Mikkelsen, EM; Taylor, KW; Hatch, EE. (2016). Exposure to multiple chemicals in a cohort of reproductive-aged Danish women. Environ Res 154: 73-85. http://dx.doi.org/10.1016/j.envres.2016.12.011.
BACKGROUND: Current exposure assessment research does not sufficiently address multi-pollutant exposure and their correlations in human media. Understanding the extent of chemical exposure in reproductive-aged women is of particular concern due to the potential for in utero exposure and fetal susceptibility.

OBJECTIVES: The objectives of this study were to characterize concentrations of chemical biomarkers during preconception and examine correlations between and within chemical classes.

METHODS: We examined concentrations of 135 biomarkers from 16 chemical classes in blood and urine from 73 women aged 18-40 enrolled in Snart Foraeldre/Milieu, a prospective cohort study of pregnancy planners in Denmark (2011-2014). We compared

biomarker concentrations with United States similarly-aged, non-pregnant women who participated in the National Health and Nutrition Environmental Survey (NHANES) and with other international biomonitoring studies. We performed principal component analysis to examine biomarker correlations.

RESULTS: The mean number of biomarkers detected in the population was 92 (range: 60-108). The most commonly detected chemical classes were phthalates, metals, phytoestrogens and polycyclic aromatic hydrocarbons. Except blood mercury, urinary barium and enterolactone, geometric means were higher in women from NHANES. Chemical classes measured in urine generally did not load on a single component, suggesting high between-class correlation among urinary biomarkers, while there is high within-class correlation for biomarkers measured in serum and blood.

CONCLUSIONS: We identified ubiquitous exposure to multiple chemical classes in reproductive-aged Danish women, supporting the need for more research on chemical mixtures during preconception and early pregnancy. Inter- and intra-class correlation between measured biomarkers may reflect common exposure sources, specific lifestyle factors or shared metabolism pathways.

hero.3479555

Russo, MV; Avino, P; Notardonato, I. (2016). Fast analysis of phthalates in freeze-dried baby foods by ultrasound-vortex-assisted liquid-liquid microextraction coupled with gas chromatography-ion trap/mass spectrometry. J Chromatogr A 1474: 1-7. http://dx.doi.org/10.1016/j.chroma.2016.10.058.

This paper is focused on the determination of phthalates (PAEs), compounds "plausibly" endocrine disruptors, in baby food products by means of a method based on ultrasound-vortex-assisted liquid-liquid microextraction coupled with GC-IT/MS (UVALLME-GC-IT/MS). Particularly, the whole procedure allows the determination of six phthalates such as DMP, DEP, DBP, iBcEP, BBP and DEHP. After dissolution of 0.1 g product sample and addition of anthracene as Internal Standard, 250 mu L of n-heptane are used as extraction solvent. The solution, held for 5 min on the vortex mixer and for 6min in an ultrasonic bath at 100W for favoring the solvent dispersion and consequently the analyte extraction, is centrifuged at 4000 rpm for 30 min. About 100 mu L of heptane are recovered and 1 mu L is injected into the GC-IT/MS. All the analytical parameters investigated are deeply discussed: under the best conditions, the percentage recoveries range between 96.2 and 109.2% with an RSD <= 10.5% whereas the Limit of Detections (LODs) and the Limit of Quantifications (LOQs) are below 11 and 20 ng g(-1), respectively, for all the PAEs except for iBcEP (23 and 43 ng g(-1), respectively). The linear dynamic range of this procedure is between 10 and 5000 ng g(-1) with R-2 >= 0.92. The method has been applied to real commercial freeze-dried samples (chicken and turkey meats) available on the Italian pharmaceutical market: three PAEs were preliminary identified, i.e. DEP (14 ng g(-1)), DBP (11 ng g(-1)) and DEHP (64 ng g(-1)). (C) 2016 Published by Elsevier B.V.

hero.3469463

Rutkowska, AZ; Diamanti-Kandarakis, E. (2016). Polycystic ovary syndrome and environmental toxins [Review]. Fertil Steril 106: 948-958. http://dx.doi.org/10.1016/j.fertnstert.2016.08.031.

Polycystic ovary syndrome (PCOS) is the most common, heterogeneous, and multifactorial endocrine disorder in premenopausal women. The pathophysiology of this endocrinopathy is still unclear; however, the heterogeneity of its features within ethnic races, geographic location, and families suggests that environment and lifestyle are of prime importance. This work is mainly focused on the possible role of the most common and studied environmental toxins for this syndrome in the pathogenesis of PCOS. Plasticizers, such as bisphenol A (BPA) or phthalates, which belong to the categories of endocrine disrupting chemicals (EDCs) and advanced glycation end products (AGEs), affect humans' health in everyday, industrialized life; therefore special attention should be paid to such exposure. Timing of exposure to EDCs is crucial for the intensity of adverse health effects. It is now evident that fetuses, infants, and/or young children are the most susceptible groups, especially in the early development periods. Prenatal exposure to EDCs that mimic endogenous hormones may contribute to the altered fetal programming and in consequence lead to PCOS and other adverse health effects, potentially transgenerationally. Acute or prolonged exposure to EDCs and AGEs through different life cycle stages may result in destabilization of the hormonal homeostasis and lead to disruption of reproductive functions. They may also interfere with metabolic alterations such as obesity, insulin resistance, and compensatory hyperinsulinemia that can exacerbate the PCOS phenotype and contribute to PCOS consequences such as type 2 diabetes and cardiovascular disease. Since wide exposure to environmental toxins and their role in the pathophysiology of PCOS are supported by extensive data

derived from diverse scientific models, protective strategies and strong recommendations should be considered to reduce human exposure to protect present and future generations from their adverse health effects.

hero.3350317

Saillenfait, AM; Ndiaye, D; Sabaté, JP; Denis, F; Antoine, G; Robert, A; Rouiller-Fabre, V; Moison, D. (2016). Evaluation of the effects of deltamethrin on the fetal rat testis. J Appl Toxicol 36: 1505-1515. http://dx.doi.org/10.1002/jat.3310.

Pregnant Sprague-Dawley rats were administered deltamethrin, at doses 0.1, 1, 5 or 10 mg kg(-1) day(-1) , or di-n-hexyl phthalate (DnHP) (250 mg kg(-1) day(-1)), by gavage, from gestational day 13 to 19. Maternal toxicity was observed at 10 mg kg(-1) day(-1) , as evidenced by transient clinical signs of neurotoxicity and reductions in body weight, body weight gain and corrected weight gain. Deltamethrin had no statistically significant effect on the incidence of post-implantation loss, fetal weight or anogenital distance in the male fetuses. Unlike DnHP, deltamethrin induced no changes in the expression of several genes involved in cholesterol transport or in the steroid synthesis pathway in the testes of gestational day 19.5 male fetuses (SRB1, StAR, P450scc, 3βHSD, P450 17 A1, 17βHSD). Fetal testicular levels of P450scc and P450 17 A1 protein were also unaffected by deltamethrin. No statistically significant differences were observed in the ex vivo fetal testicular production of testosterone and androstenedione after deltamethrin exposure, whereas DnHP markedly reduced these parameters. The deltamethrin metabolite, 3-phenoxybenzoic acid, was detected in amniotic fluid. In summary, our results demonstrate that in utero exposure to deltamethrin during the period of sexual differentiation had no significant effect on the testosterone synthesis pathway in the male rat fetus up to a maternal toxic dose. Copyright 2016 John Wiley & Sons, Ltd.

hero.3469466

Saini, A; Okeme, JO; Mark Parnis, J; Mcqueen, RH; Diamond, ML. (2016). From air to clothing: characterizing the accumulation of semi-volatile organic compounds to fabrics in indoor environments. Indoor Air. http://dx.doi.org/10.1111/ina.12328.

Uptake kinetics of semi-volatile organic compounds (SVOCs) present indoors, namely phthalates and halogenated flame retardants (HFRs), were characterized for cellulose-based cotton and rayon fabrics. Cotton and rayon showed similar accumulation of gas- and particle-phase SVOCs, when normalized to planar surface area. Accumulation was 3-10 times greater by rayon than cotton, when normalized to Brunauer-Emmett-Teller (BET) specific surface area which suggests that cotton could have a longer linear uptake phase than rayon. Linear uptake rates of eight consistently detected HFRs over 56 days of 0.35-0.92m(3) /day.dm(2) planar surface area and mass transfer coefficients of 1.5-3.8m/h were statistically similar for cotton and rayon and similar to those for uptake to passive air sampling media. These results suggest air-side controlled uptake and that, on average, 2m(2) of clothing typically worn by a person would sequester the equivalent of the chemical content in 100m(3) of air per day. Distribution coefficients between fabric and air (K') ranged from 6.5 to 7.7 (log K') and were within the range of partition coefficients measured for selected phthalates as reported in the literature. The distribution coefficients were similar for low molecular weight HFRs, and up to two orders of magnitude lower than the equilibrium partition coefficients estimated using the COSMO-RS model. Based on the COSMO-RS model, time to reach 95% of equilibrium for PBDEs between fabric and gas-phase compounds ranged from 0.1 to >10years for low to high molecular weight HFRs.

hero.3462778

Saini, A; Thaysen, C; Jantunen, L; Mcqueen, RH; Diamond, ML. (2016). From Clothing to Laundry Water: Investigating the Fate of Phthalates, Brominated Flame Retardants, and Organophosphate Esters. Environ Sci Technol 50: 9289-9297. http://dx.doi.org/10.1021/acs.est.6b02038.

The accumulation of phthalate esters, brominated flame retardants (BFRs) and organophosphate esters (OPEs) by clothing from indoor air and transfer via laundering to outdoors were investigated. Over 30 days cotton and polyester fabrics accumulated 3475 and 1950 ng/dm(2) 5phthalates, 65 and 78 ng/dm(2) 10BFRs, and 1200 and 310 ng/dm(2) 8OPEs, respectively. Planar surface area concentrations of OPEs and low molecular weight phthalates were significantly greater in cotton than polyester and similar for BFRs and high molecular weight phthalates. This difference was significantly and inversely correlated with KOW, suggesting

greater sorption of polar compounds to polar cotton. Chemical release from cotton and polyester to laundry water was >80% of aliphatic OPEs (log KOW < 4), < 50% of OPEs with an aromatic structure, 50-100% of low molecular weight phthalates (log KOW 4-6), and < detection-35% of higher molecular weight phthalates (log KOW > 8) and BFRs (log KOW > 6). These results support the hypothesis that clothing acts an efficient conveyer of soluble semivolatile organic compounds (SVOCs) from indoors to outdoors through accumulation from air and then release during laundering. Clothes drying could as well contribute to the release of chemicals emitted by electric dryers. The results also have implications for dermal exposure.

hero.3469369

Saini, G; Pant, S; Singh, SO; Kazmi, AA; Alam, T. (2016). A comparative study of occurrence and fate of endocrine disruptors: diethyl phthalate and dibutyl phthalate in ASP- and SBR-based wastewater treatment plants. Environ Monit Assess 188: 609. http://dx.doi.org/10.1007/s10661-016-5617-4.

Phthalates are endocrine-disrupting chemicals which affect endocrine system by bio-accumulation in aquatic organisms and produce adverse health effects in aquatic organisms as well as human beings, when come in contact. Present study focuses on occurrence and removal of two phthalates: diethylphthalate (DEP) and dibutylphthalate (DBP) in two full-scale wastewater treatment plants (WWTPs) i.e. sewage treatment plants (STPs) based on well-adopted technologies, activated sludge process (ASP) and sequencing batch reactor (SBR).Gas chromatography-mass spectrometry (GC-MS) analysis was performed for both wastewater and sludge sample for determination and identification of the concentration of these compounds in both STPs by monitoring the STPs for 9months. It was observed that the concentration of DEP was less than DBP in the influent of ASP and SBR. Average concentrations of DEP and DBP in sludge sample of ASP were found to be 2.15 and 2.08ng/g, whereas in SBR plant, these values were observed as 1.71 and 2.01ng/g, respectively. Concerning the removal efficiency of DEP, SBR and ASP plants were found effective with removal efficiency of 91.51 and 91.03%, respectively. However, in the case of DBP, SBR showed lower removal efficiency (85.42%) as compared to ASP (92.67%). Comparative study of both plants proposed that in ASP plant, DBP reduction was higher than the SBR. Fourier transformation infrared (FTIR) analysis also confirmed the same result of sludge analysis for both STPs. Sludge disposal studied with scanning electron microscopy (SEM), energy dispersive X-ray spectroscopy (EDX) and thermo-gravimetric analysis (TGA) techniques confirmed that sludge of both STPs have high calorific value and can be used as fuel to make fuel-briquettes and bottom ash to make firebricks.

hero.3350231

Salamin, O; De Angelis, S; Tissot, JD; Saugy, M; Leuenberger, N. (2016). Autologous Blood Transfusion in Sports: Emerging Biomarkers [Review]. Transfus Med Rev 30: 109-115. http://dx.doi.org/10.1016/j.tmrv.2016.05.007.

Despite being prohibited by the World Anti-Doping Agency, blood doping through erythropoietin injection or blood transfusion is frequently used by athletes to increase oxygen delivery to muscles and enhance performance. In contrast with allogeneic blood transfusion and erythropoietic stimulants, there is presently no direct method of detection for autologous blood transfusion (ABT) doping. Blood reinfusion is currently monitored with individual follow-up of hematological variables via the athlete biological passport, which requires further improvement. Microdosage is undetectable, and suspicious profiles in athletes are often attributed to exposure to altitude, heat stress, or illness. Additional indirect biomarkers may increase the sensitivity and specificity of the longitudinal approach. The emergence of "-omics" strategies provides new opportunities to discover biomarkers for the indirect detection of ABT. With the development of direct quantitative methods, transcriptomics based on microRNA or messenger RNA expression is a promising approach. Because blood donation and blood reinfusion alter iron metabolism, quantification of proteins involved in metal metabolism, such as hepcidin, may be applied in an "ironomics" strategy to improve the detection of ABT. As red blood cell (RBC) storage triggers changes in membrane proteins, proteomic methods have the potential to identify the presence of stored RBCs in blood. Alternatively, urine matrix can be used for the quantification of the plasticizer di(2-ethyhexyl)phthalate and its metabolites that originate from blood storage bags, suggesting recent blood transfusion, and have an important degree of sensitivity and specificity. This review proposes that various indirect biomarkers should be applied in combination with mathematical approaches for longitudinal monitoring aimed at improving ABT detection.

hero.3455107

Sampath, S; Selvaraj, KK; Shanmugam, G; Krishnamoorthy, V; Chakraborty, P; Ramaswamy, BR. (2016). Evaluating spatial distribution and seasonal variation of phthalates using passive air sampling in southern India. Environ Pollut. http://dx.doi.org/10.1016/j.envpol.2016.12.003.

Usage of phthalates as plasticizers has resulted in worldwide occurrence and is becoming a serious concern to human health and environment. However, studies on phthalates in Indian atmosphere are lacking. Therefore, we studied the spatio-temporal trends of six major phthalates in Tamil Nadu, southern India, using passive air samplers. Phthalates were ubiquitously detected in all the samples and the average total phthalates found in decreasing order is pre-monsoon (61ngm(-3))>summer (52ngm(-3))>monsoon (17ngm(-3)). Largely used phthalates, dibutylphthalate (DBP) and diethylhexlphthalate (DEHP) were predominantly found in all the seasons with contribution of 11-31% and 59-68%, respectively. The highest total phthalates was observed in summer at an urban location (836ngm(-3)). Furthermore, through principal component analysis, potential sources were identified as emissions from additives of plasticizers in the polymer industry and the productions of adhesives, building materials and vinyl flooring. Although inhalation exposure of infants was higher than other population segments (toddlers, children and adults), exposure levels were found to be safe for people belonging to all ages based on reference dose (RfD) and tolerable daily intake (TDI) values. This study first attempted to report seasonal trend based on atmospheric monitoring using passive air sampling technique and exposure risk together.

hero.3469377

Sathyanarayana, S; Barrett, E; Nguyen, R; Redmon, B; Haaland, W; Swan, SH. (2016). First Trimester Phthalate Exposure and Infant Birth Weight in the Infant Development and Environment Study. Int J Environ Res Public Health 13. http://dx.doi.org/10.3390/ijerph13100945.

Phthalate exposure is widespread among pregnant women but whether it is related to fetal growth and birth weight remains to be determined. We examined whether first trimester prenatal phthalate exposure was associated with birth weight in a pregnancy cohort study. We recruited first trimester pregnant women from 2010-2012 from four centers and analyzed mother/infant dyads who had complete urinary phthalate and birth record data (N = 753). We conducted multiple linear regression to examine if prenatal log specific gravity adjusted urinary phthalate exposure was related to birthweight in term and preterm (37 weeks) infants, stratified by sex. We observed a significant association between mono carboxy-isononyl phthalate (MCOP) exposure and increased birthweight in term males, 0.13 kg (95% CI 0.03, 0.23). In preterm infants, we observed a 0.49 kg (95% CI 0.09, 0.89) increase in birthweight in relation to a one log unit change in the sum of di-ethylhexyl phthalate (DEHP) metabolite concentrations in females (N = 33). In summary, we observed few associations between prenatal phthalate exposure and birthweight. Positive associations may be attributable to unresolved confounding in term infants and limited sample size in preterm infants.

hero.3469345

Sathyanarayana, S; Grady, R; Barrett, ES; Redmon, B; Nguyen, RH; Barthold, JS; Bush, NR; Swan, SH. (2016). First trimester phthalate exposure and male newborn genital anomalies. Environ Res 151: 777-782. http://dx.doi.org/10.1016/j.envres.2016.07.043.

BACKGROUND: Anti-androgenic phthalates are environmental chemicals that affect male genital development in rodents leading to genitourinary birth defects. We examined whether first trimester phthalate exposure may exert similar effects in humans leading to an increased incidence of newborn male genital anomalies in a multi-center cohort study.

METHODS: We recruited first trimester pregnant women within The Infant Development and the Environment Study (TIDES) from 2010 to 2012 from four study centers and limited analyses to all mother/male infant dyads who had complete urinary phthalate and birth exam data (N=371). We used multivariate logistic regression to determine the odds of having a genital anomaly in relation to phthalate exposure.

RESULTS: Hydrocele was the primary abnormality observed in the cohort (N=30) followed by undescended testes (N=5) and hypospadias (N=3). We observed a statistically significant 2.5 fold increased risk (95% CI 1.1, 5.9) of having any anomaly and 3.0 fold increased risk (95% CI 1.2, 7.6) of isolated hydrocele in relation to a one log unit increase in the sum of di-ethylhexyl phthalate (DEHP) metabolites.

CONCLUSIONS: First trimester urinary DEHP metabolite concentrations were associated with increased odds of any newborn genital anomaly, and this association

was primarily driven by isolated hydrocele which made up the majority of anomalies in newborn males. The association with hydrocele has not been previously reported and suggests that it may be an endpoint affected by prenatal phthalate exposures in the first trimester of development. Future human studies should include hydrocele assessment in order to confirm findings.

hero.3350324

Schmitt, EE; Vellers, HL; Porter, WW; Lightfoot, JT. (2016). Environmental endocrine disruptor affects voluntary physical activity in mice. Med Sci Sports Exer 48: 1251-1258. http://dx.doi.org/10.1249/MSS.0000000000000908.
INTRODUCTION: Voluntary physical activity levels are regulated by sex hormones. The purpose of this study was to determine the effect of the endocrine disruptor benzyl butyl phthalate (BBP) on the regulation of physical activity in mice.

METHODS: Mouse dams were treated with 500 mgkgd of BBP or vehicle on gestation days 9-16. Pups were weaned and analyzed for voluntary physical activity levels, puberty development, sex hormone levels, and body composition during the 20-wk period.

RESULTS: Seventy-three offspring from BBP-treated dams were studied (n = 43 males and n = 30 females). Endocrine disruption was indicated by decreased anogenital distances in BBP-treated male offspring at 10 (P = 0.001) and 20 wk (P = 0.038) and delayed vaginal openings in BBP-treated female offspring (P = 0.001). Further, there was a significant decrease in serum testosterone concentration in male mice between control and BBP at 10 wk (P = 0.039) and at 20 wk (P = 0.022). In female mice, there was a significant increase in serum testosterone concentration in BBP mice at 20 wk (P = 0.002) and a significant increase in estrogen (estradiol) concentrations at 20 wk in the control female mice (P = 0.015). Overall, BBP mice ran significantly less distance (males, P = 0.008; females, P = 0.042) than controls. Other than a significant increase in BBP-treated males in fat mass at 20 wk (P = 0.040), there was no significant decrease in weight, lean mass, or fat mass in either female or male mice, regardless of treatment.

CONCLUSION: Maternal endocrine disruption altered hormone response, but not body composition in either sex of offspring, with a corresponding decreased activity throughout early adulthood in all offspring. These results suggest that exposure to common environmental endocrine disruptors in utero can reduce and alter physical activity levels in offspring.

hero.3479504

Selvaraj, KK; Mubarakali, H; Rathinam, M; Harikumar, L; Sampath, S; Shanmugam, G; Ramaswamy, BR. (2016). Cumulative exposure and dietary risk assessment of phthalates in bottled water and bovine milk samples: A preliminary case study in Tamil Nadu, India. Hum Ecol Risk Assess 22: 1166-1182. http://dx.doi.org/10.1080/10807039.2016.1146984.
Exposure to phthalates may cause adverse health effects in wildlife and humans. Study on phthalates exposure and risk is limited in the Indian context. Therefore, this preliminary investigation was performed to ascertain the phthalates exposure through bottled water and milk among the Indian sub-population. Phthalates were extracted from water and milk by solid-phase and ultrasonication methods, respectively, and analysis was performed using gas chromatography-mass spectrometry. Total phthalates in bottled water and milk were in the range of 39-7820ng/L and 56-686ng/g, respectively, with the highest contribution from diethylhexyl phthalate (DEHP). A substantial increase in phthalates concentration in bottled water was observed with increased shelf life. Total mean phthalates in packed milk (245ng/g) and raw milk (134ng/g) shows potential enrichment during farm to table process. Among phthalates, the lowest risk was expected from diethyl phthalate, whereas the highest risk was observed for DEHP with cumulative dietary exposure of 0.23g/kgbw/day (median). The human health risk based on tolerable daily intake and reference dose was found safe. This is the first study reporting phthalates migration in packed commodities from a developing country, India, which further warrants extensive phthalates exposure assessment to understand its effect on public health.

hero.3070938

Serrano, K; Levin, E; Chen, D; Hansen, A; Turner, TR; Kurach, J; Reidel, A; Boecker, WF; Acker, JP; Devine, DV. (2015). An investigation of red blood cell concentrate quality during storage in paediatric-sized polyvinylchloride bags plasticized with alternatives to di-2-ethylhexyl phthalate (DEHP). Vox Sang 110: 227-235. http://dx.doi.org/10.1111/vox.12355.
BACKGROUND AND OBJECTIVES: Di-2-ethylhexyl phthalate (DEHP) is a blood bag

plasticizer. It is also a toxin, raising concerns for vulnerable populations, for example, neonates and infants. Here, the in vitro quality of red cell concentrates (RCC) stored in paediatric bags formulated with alternative plasticizers to DEHP was compared.

MATERIALS AND METHODS: RCC were pooled and split into polyvinylchloride (PVC)/DEHP, PVC/1,2-cyclohexanedicarboxylic acid diisononyl ester (DINCH) or PVC/butyryl trihexyl citrate (BTHC) bags. Quality was assessed on storage days 5, 21, 35 and 43.

RESULTS: Metabolism differed among the bags: pCO2 levels were lowest and pO2 were highest in BTHC bags. Glucose consumption and lactate production suggested higher metabolic rates in BTHC bags. ATP levels were best maintained in DINCH bags (day 43 mean level: 286 029 µmol/g Hb). RCC in BTHC bags had the greatest potassium release (546 30 mm on day 43). From day 21, haemolysis was higher in BTHC bags (P < 001) and by day 43 had exceeded 08% (085 010%). RCC in BTHC bags showed more microparticle formation than RCC in DEHP or DINCH bags.

CONCLUSION: The results suggest that the BTHC formulation used was detrimental to RBC quality. DINCH bags could be a viable alternative to DEHP: they outperformed DEHP bags energetically, with better maintenance of ATP levels.

hero.3469366

Sheikh, IA; Abu-Elmagd, M; Turki, RF; Damanhouri, GA; Beg, MA; Al-Qahtani, M. (2016). Endocrine disruption: In silico perspectives of interactions of di-(2-ethylhexyl)phthalate and its five major metabolites with progesterone receptor. BMC Struct Biol 16: 16. http://dx.doi.org/10.1186/s12900-016-0066-4.
BACKGROUND: Di-(2-ethylhexyl)phthalate (DEHP) is a common endocrine disrupting compound (EDC) present in the environment as a result of industrial activity and leaching from polyvinyl products. DEHP is used as a plasticizer in medical devices and many commercial and household items. Exposure occurs through inhalation, ingestion, and skin contact. DEHP is metabolized to a primary metabolite mono-(2-ethylhexyl)phthalate (MEHP) in the body, which is further metabolized to four major secondary metabolites, mono(2-ethyl-5-hydroxyhexyl)phthalate (5-OH-MEHP), mono(2-ethyl-5-oxyhexyl)phthalate (5-oxo-MEHP), mono(2-ethyl-5-carboxypentyl)phthalate (5-cx-MEPP) and mono[2-(carboxymethyl)hexyl]phthalate (2-cx-MMHP). DEHP and its metabolites are associated with developmental abnormalities and reproductive dysfunction within the human population. Progesterone receptor (PR) signaling is involved in important reproductive functions and is a potential target for endocrine disrupting activities of DEHP and its metabolites. This study used in silico approaches for structural binding analyses of DEHP and its five indicated major metabolites with PR.

METHODS: Protein Data bank was searched to retrieve the crystal structure of human PR (Id: 1SQN). PubChem database was used to obtain the structures of DEHP and its five metabolites. Docking was performed using Glide (Schrodinger) Induced Fit Docking module.

RESULTS: DEHP and its metabolites interacted with 19-25 residues of PR with the majority of the interacting residues overlapping (82-95% commonality) with the native bound ligand norethindrone (NET). DEHP and each of its five metabolites formed a hydrogen bonding interaction with residue Gln-725 of PR. The binding affinity was highest for NET followed by DEHP, 5-OH-MEHP, 5-oxo-MEHP, MEHP, 5-cx-MEPP, and 2-cx-MMHP.

CONCLUSION: The high binding affinity of DEHP and its five major metabolites with PR as well as a high rate of overlap between PR interacting residues among DEHP and its metabolites and the native ligand, NET, suggested their disrupting potential in normal PR signaling, resulting in adverse reproductive effects.

hero.3469363

Sheikh, IA; Yasir, M; Abu-Elmagd, M; Dar, TA; Abuzenadah, AM; Damanhouri, GA; Al-Qahtani, M; Beg, MA. (2016). Human sex hormone-binding globulin as a potential target of alternate plasticizers: an in silico study. BMC Struct Biol 16: 15. http://dx.doi.org/10.1186/s12900-016-0067-3.
BACKGROUND: Currently, alternate plasticizers are used to replace phthalate plasticizers in children's toys, medical equipments and food packaging, due to the adverse effects of phthalate compounds on human health and laws prohibiting their use. Current information regarding the safety and potential adverse effects of alternate plasticizers is limited and recent studies have found alternate plasticizers to display similar characteristics to those observed in phthalate plasticizers. This study was undertaken to evaluate and predict the potential endocrine disrupting activity of the three most commonly used alternate plasticizers: di(2-ethylhexyl)terephthalate (DEHT), tris(2-ethylhexyl)trimellitate (TOTM), and

diisononyl hexahydrophthalate (DINCH) against human sex hormone-binding globulin (SHBG) using in silico approaches.

MATERIALS AND METHODS: The crystal structure of human SHBG (Id: 1D2S) was retrieved from Protein Data Bank. PubChem database was searched for the structures of alternate plasticizers, DEHT, TOTM, and DINCH. Docking was performed using Glide (Schrodinger) Induced Fit Docking module.

RESULTS: Induced Fit Docking of three alternate plasticizer compounds indicated that each of the three compounds fitted well into the steroid binding pocket of SHBG. Docking displays showed interactions of alternate plasticizers with 25-30 amino-acid residues of SHBG; 18-20 amino residues overlapped between the natural ligand, DHT, and the three compounds (commonality of 82-91%). The hydrogen-bonding interaction of the amino-acid residue, Asn-82, of SHBG was also present in displays of DHT and all the three alternate phthalates. The binding affinity of all the three alternate phthalates was higher than DHT; maximum in DINCH followed by TOTM and DEHT.

CONCLUSION: Our results suggested that the three alternate plasticizers have potential to engage the important interacting residues of SHBG and thus interfere in its steroid homeostatic function.

hero.3466587

Shen, R; Zhao, LL; Yu, Z; Zhang, C; Chen, YH; Wang, H; Zhang, ZH; Xu, DX. (2016). Maternal di-(2-ethylhexyl) phthalate exposure during pregnancy causes fetal growth restriction in a stage-specific but gender-independent manner. Reprod Toxicol 67: 117-124. http://dx.doi.org/10.1016/j.reprotox.2016.12.003.

Di (2-ethylhexyl) phthalate (DEHP) is male developmental toxicant that impairs testis development with reduced anogenital distance. The present study aimed to investigate whether maternal DEHP exposure during pregnancy causes intrauterine growth restriction (IUGR) in a gender-specific manner and to identify the critical window of DEHP-induced fetal IUGR. Pregnant mice were administered with DEHP (0, 50 or 200mg/kg) by gavage. Fetal IUGR was observed not only in males but also in females when litters were exposed to DEHP on gestational day (GD)0-GD17. Interestingly, fetal weight and crown-rump length were reduced, markedly in dams with DEHP on GD13-GD17, slightly in dams with on GD7-GD12, but not in dams with on GD0-GD6. Further analysis showed that maternal DEHP exposure on GD7-GD12 inhibited cell proliferation, lowered placental weight, and reduced blood sinusoid area in placental labyrinth layer. These results suggest that maternal DEHP exposure induces IUGR in a stage-specific but gender-independent manner.

hero.3479543

Shi, LK, ai; Zhang, MM; Liu, Y, uLan. (2016). Concentration and survey of phthalic acid esters in edible vegetable oils and oilseeds by gas chromatography-mass spectrometry in China. Food Control 68: 118-123. http://dx.doi.org/10.1016/j.foodcont.2016.03.027.

Now, there is a lack of information regarding the occurrence and the content of phthalic acid esters (PAEs) contamination in edible vegetable oils and oilseeds used for oil production in China. In this study, a method for determination of five PAEs was developed based on gas chromatography-mass spectrometry. Method recoveries for oils and oilseeds were 72.4-103.0% and 77.2-98.8%, respectively. RSDs of five analytes in oils and oilseeds were ranging from 1.22 to 8.64% and 0.62-9.37%, respectively. The LODs and LOQs were ranging from 0.10 to 0.79 and 0.33-2.60 mu g/kg, respectively. Based on the established method, PAE concentrations in thirty-four edible oils and twenty-eight oilseeds were evaluated. Five and thirteen oil samples exceeded the upper limits 1.5 and 0.3 mg/kg set for di(2-ethtlhexyl) phthalate and dibutyl phthalate in China, respectively. The results obtained indicated that more concern and comprehensive legislation are still needed and mulriple issues should be considered when it comes to the PAEs contamination in edible vegetable oils. (c) 2016 Elsevier Ltd. All rights reserved.

hero.3469215

Shiue, I. (2016). Urinary arsenic, pesticides, heavy metals, phthalates, polyaromatic hydrocarbons, and polyfluoroalkyl compounds are associated with sleep troubles in adults: USA NHANES, 2005-2006. Environ Sci Pollut Res. http://dx.doi.org/10.1007/s11356-016-8054-6.

Links between environmental chemicals and human health have emerged, but the effects on sleep health were less studied. Therefore, the aim of the present study was to investigate the relationships of different sets of environmental chemicals and common sleep troubles in a national and population-based setting.

Data were retrieved from the United States National Health and Nutrition Examination Surveys, 2005-2006 including demographics, serum measurements, lifestyle factors, self-reported sleep troubles, and urinary environmental chemical concentrations. Statistical analyses including descriptive statistics, t-test, chi-square test, and survey-weighted logistic regression models were performed. Of all 5563 Americans aged 18-85, 2331 (42.0%) had wake-up at night, 2914 (52.5%) felt unrested during the day, 740 (13.4%) had leg jerks while sleeping, and 1059 (19.1%) had leg cramps for 2+ times a month. Higher levels of urinary arsenic, phthalates, and polyfluoroalkyl compounds were associated with wake-up at night. Higher levels of urinary 4-tert-octylphenol and polyfluoroalkyl compounds were associated with being unrested during the day. Higher levels of urinary arsenic, polyaromatic hydrocarbons, and polyfluoroalkyl compounds were associated with leg jerks while sleeping. Higher levels of urinary pesticides, heavy metals, phthalates, and polyaromatic hydrocarbons were associated with leg cramps while sleeping. However, there were no significant associations with other environmental chemicals such as parabens, bisphenol A, benzophenone-3, triclosan, perchlorate, nitrate, or thiocyanate. Eliminating arsenic, heavy metals, phthalate, pesticides, polyaromatic hydrocarbons, and polyfluoroalkyl compounds to improve sleep health might be considered while understanding the biological pathway with a longitudinal or experimental approach in future research would be suggested.

hero.3445429

Shiue, I. (2016). Urinary polyaromatic hydrocarbons are associated with adult emphysema, chronic bronchitis, asthma, and infections: US NHANES, 2011-2012. Environ Sci Pollut Res 23: 25494-25500. http://dx.doi.org/10.1007/s11356-016-7867-7.

Links between environmental chemicals and human health have emerged over the last few decades, but the effects from polyaromatic hydrocarbons were less studied, compared to other commonly known environmental chemicals such as heavy metals, phthalates, arsenic, phenols, pesticides, etc. Therefore, the aim of the study was to examine the relationships of urinary polyaromatic hydrocarbons and adult respiratory health conditions using a large human sample in a national and population-based setting in recent years. Data were retrieved from United States National Health and Nutrition Examination Surveys, 2011-2012 including demographics, self-reported health conditions, and urinary polyaromatic hydrocarbons. Statistical analyses including chi-square test, t test, and survey-weighted logistic regression modeling were performed. Of 5560 American adults aged 20-80, urinary 2-hydroxyfluorene and 3-hydroxyfluorene were positively associated with emphysema (OR, 1.60, 95% CI 1.26 to 2.03, P=0.001 and OR, 1.42, 95% CI 1.15 to 1.77, P=0.003, respectively) and chronic bronchitis (OR, 1.42, 95% CI 1.04 to 1.94, P=0.031 and OR, 1.40, 95% CI 1.03 to 1.91, P=0.036, respectively), while 2-hydroxynaphthalene (2-naphthol) was likely to be borderline associated with emphysema and chronic bronchitis. Conversely, urinary 1-hydroxyphenanthrene, 3-hydroxyphenanthrene, 1-hydroxypyrene, and 4-hydroxyphenanthrene were inversely associated with asthma and infections. Urinary polyaromatic hydrocarbons are associated with adult respiratory health conditions, although the causality cannot be established. For future research, studies using large human sample across regions to longitudinally monitor would be suggested. For practice and policy-making, regulation on minimizing polyaromatic hydrocarbons exposure to protect respiratory health might need to be considered in future health and environmental policies and intervention programs.

hero.3469474

Shrestha, R; Palat, A; Punnoose, AM; Joshi, S; Ponraju, D; Paul, SF. (2016). Electrospun cellulose acetate phthalate nanofibrous scaffolds fabricated using novel solvent combinations biocompatible for primary chondrocytes and neurons. Tissue Cell 48: 634-643. http://dx.doi.org/10.1016/j.tice.2016.07.007.

Electrospun nanofibres have been shown to exhibit extracellular matrix (ECM)-like characteristics required for tissue engineering in terms of porosity, flexibility, fibre organization and strength. This study focuses on developing novel cellulose acetate phthalate (CAP) scaffolds by electrospinning for establishing 3-D chondrocyte and neuronal cultures. Five solvent combinations were employed in fabricating the fibres, namely, acetone/ethanol (9:1), dimethylformamide/tetrahydrofuran/acetone (3:3:4), tetrahydrofuran/acetone (1:1), tetrahydrofuran/ethanol (1:1) and chloroform/methanol (1:1). The electrospun fibres were characterized by scanning electron microscopy (SEM) analysis and confirmed to be within the nanometre range. Based on the morphology of the fibers from SEM results, two solvent combinations such as acetone/ethanol and dimethylformamide/tetrahydrofuran/acetone were selected for stabilization as CAP exhibits a pH dependent

solubility. Fourier-Transform Infrared (FTIR) analysis revealed the hydrolysis of CAP which was overcome by EDC [1-ethyl-3-(3-dimethylaminopropyl) carbodiimide] and EDC/NHS (N-hydroxysuccinimide) cross-linking resulting in its stability (pH of 7.2) for three months. MTT [3-(4, 5-dimethylthiazol-2-yl)-1, 5-diphenyltetrazolium bromide] assay performed using L6 myoblast confirmed the biocompatibility of the scaffolds. 3-D primary chondrocyte and neuronal cultures were established on the scaffolds and maintained for a period of 10 days. H&E staining and SEM analysis showed the attachment of the chondrocytes and neurons on CAP scaffolds prepared using dimethylformamide/tetrahydrofuran/acetone and acetone/ethanol respectively.

hero.3469355

Simon, C; Onghena, M; Covaci, A; Van Hoeck, E; Van Loco, J; Vandermarken, T; Van Langenhove, K; Demaegdt, H; Mertens, B; Vandermeiren, K; Scippo, ML; Elskens, M. (2016). Screening of endocrine activity of compounds migrating from plastic baby bottles using a multi-receptor panel of in vitro bioassays. Toxicol in Vitro 37: 121-133. http://dx.doi.org/10.1016/j.tiv.2016.09.008.

Endocrine activity of 65 compounds migrating from polycarbonate replacement plastic baby bottles was assessed using in vitro cell based assays (reporter gene assays) involving 7 nuclear receptors, i.e. human steroid hormones receptors (oestrogen, androgen, progesterone and glucocorticoid receptors), human thyroid beta and peroxisome proliferator-activated gamma receptors, and the mouse aryl hydrocarbon receptor. The chemicals were tested at 4 concentrations ranging from 0.001mM to 1mM. Only twelve chemicals did not show any activity towards any of the nuclear receptors, while fifty three compounds showed a possible endocrine activity. Most of the agonistic activities were observed towards the oestrogen receptor while the PPARγ was the target for most of the recorded antagonistic activities. Agonistic activities were recorded for several phthalates, benzophenones, aromatic hydrocarbons and phenols, while compounds such as benzaldehydes, ketones and esters of fatty acid showed antagonistic activities. Thirty five chemicals were able of agonistic activities on 1 to 4 receptors and antagonistic activities were recorded for 35 compounds as well, towards 1 to 7 receptors. Sixteen compounds were able of both agonistic and antagonistic activities, but not on the same receptors, except in 2 cases for the oestrogen receptor and 4 cases for the PPARγ.

hero.3102509

Singal, AK; Jain, VG. (2016). Maternal and infant characteristics influencing the anogenital distance and penile length in newborns. Andrologia 48: 708-713. http://dx.doi.org/10.1111/and.12507.

Recent studies have suggested that maternal characteristics can affect reproductive health of offspring, possibly through pre-natal hormonal influence. Anogenital distance (AGD) is an anthropometric measure which is a sensitive reproductive endpoint of masculinisation. It provides a read-out of pre-natal androgen exposure and has been associated with several reproductive health outcomes in humans. We studied AGD and stretched penile length (SPL) in a large, racially homogenous sample of consecutive newborns to understand their association with maternal and infant characteristics. A prospective cross-sectional study involving measurement of AGD and SPL at birth was performed by a single trained observer. A total of 1077 newborns (553 males and 524 females) were included in final anthropometric analysis. The mean AGD of males was 2.560.31cm, and the mean AGD of females was 1.54 0.17cm. The mean SPL of males was 3.310.38cm. On multiple regression analysis, for both males and females, birthweight (β=0.229, P<0.001 and β=0.135, P<0.001, respectively) was modest but significant predictor for AGD. For SPL, only gestational age (β=0.054, P<0.001) was found to be statistically significant predictor. There was no significant association observed for gravidity, parity and maternal age with both AGD and SPL. Thus, no maternal characteristics (age, gravidity, parity) influence AGD or SPL in human infants.

hero.3469539 REVIEW

Smarr, MM; Kannan, K; Buck Louis, GM. (2016). Endocrine disrupting chemicals and endometriosis [Review]. Fertil Steril 106: 959-966. http://dx.doi.org/10.1016/j.fertnstert.2016.06.034.

Endometriosis is an estrogen dependent gynecologic disease with lasting implications for many women's fertility, somatic health, and overall quality of life. Growing evidence suggests that endocrine disrupting chemicals (EDCs) may be etiologically involved in the development and severity of disease. We weigh the available human evidence focusing on EDCs and endometriosis, restricting to research that has individually

quantified chemical concentrations for women, included a comparison group of unaffected women, and used multivariable analytic techniques. Evidence supporting an environmental etiology for endometriosis includes metals/trace elements, dioxins, and other persistent organic pollutants, as well as nonpersistent chemicals, such as benzophenones and phthalates. To address the equivocal findings for various EDCs, future research directions for filling data gaps include [1] use of integrated clinical and population sampling frameworks allowing for incorporation of new diagnostic modalities; [2] the collection of various biologic media, including target tissues for quantifying exposures; [3] study designs that offer various comparison groups to assess potentially shared etiologies with other gynecologic disorders; and [4] novel laboratory and statistical approaches that fully explore all measured EDCs for the assessment of mixtures and low dose effects and the use of directed acyclic graphs and supporting causal analysis for empirically delineating relationships between EDCs and endometriosis.

hero.3469480

Sohn, J; Kim, S; Koschorreck, J; Kho, Y; Choi, K. (2016). Alteration of sex hormone levels and steroidogenic pathway by several low molecular weight phthalates and their metabolites in male zebrafish (Danio rerio) and/or human adrenal cell (H295R) line. J Hazard Mater 320: 45-54. http://dx.doi.org/10.1016/j.jhazmat.2016.08.008.
Low molecular weight phthalates, such as diethyl phthalate (DEP), benzyl butyl phthalate (BBzP), or diisobutyl phthalate (DiBP), are suspected to disrupt endocrine system. However, their adverse effects on sex steroid hormones and underlying mechanisms are not well-documented. The aim of this study is to investigate the effects of major low molecular weight phthalates (LMWPs), i.e., DEP, BBzP, and DiBP, and their hydrolytic metabolites, on sex steroid hormone system, employing male zebrafish and/or a human adrenocortical carcinoma (H295R) cell. In male zebrafish, 14-day exposure to DEP, BBzP, or DiBP significantly decreased testosterone (T) concentrations. All test compounds significantly up-regulated cyp19a gene expression, and down-regulated star and 3β hsd genes in the male fish. In H295R cell, all test compounds except monoisobutyl phthalate (MiBP) reduced T concentrations and increased E2/T ratio. Gene expression changes in H295R cell, e.g., significant down-regulation of StAR gene and up-regulation of CYP19A gene, supported depressed synthesis of sex hormones in the adrenal cell. Our results show that not only DEP, BBzP, and DiBP, but also their hydrolytic metabolites disrupt sex hormone balances through modulating key steroidogenic genes in the human adrenal cells and in zebrafish.

hero.3469516

Somasundaram, DB; Manokaran, K; Selvanesan, BC; Bhaskaran, RS. (2016). Impact of di-(2-ethylhexyl) phthalate on the uterus of adult Wistar rats. Hum Exp Toxicol. http://dx.doi.org/10.1177/0960327116657601.
Di-(2-ethylhexyl) phthalate (DEHP) is the most common plasticizer used in polyvinyl chloride-based plastics. DEHP is not covalently bound to the plastics and is easily released to the environment, resulting in human exposure. In this study, the adult rats were exposed to DEHP and its effects on the uterus was evaluated. Healthy adult female rats were treated with DEHP orally (with dose level 0, 1, 10, and 100 mg/kg body weight/day) for 30 days. No significant changes in the body weight and wet uterine weight were observed. Ovarian hormones and their receptor levels in the uterus were increased. Histological studies exhibited the structural abnormalities such as decrease in diameter, thinning of the layers and disruption in the glandular epithelium.

hero.3350327

Son, YR; Chung, JH; Ko, S; Shim, SM. (2016). Combinational enhancing effects of formulation and encapsulation on digestive stability and intestinal transport of green tea catechins. J Microencapsulation 33: 183-190. http://dx.doi.org/10.3109/02652048.2016.1144816.
The hypothesis was that green tea catechins (GTCs) formulated with vitamin C and xylitol followed by enteric coating with hydroxypropyl methyl cellulose phthalate (HPMCP) or encapsulated into γ-cyclodextrin (γ-CD) could enhance intestinal absorption of GTCs. Surface morphology and size obtained by SEM were different. Digestive stability of GTCs encapsulated into γ-CD or coated with HPMCP was enhanced up to 65.56% or 57.63%, respectively. When GTCs were formulated, the digestive stability was greater than the one not formulated. Formulated GTCs followed by encapsulation into γ-CD significantly increased intestinal transport. Absorption of GTCs was 2.8%, 9.64%, 11.97%, 8.41% and 14.36% for only GTCs, GTCs encapsulated into γ-CD, formulated GTCs encapsulated into γ-CD, GTCs coated with HPMCP and formulated GTCs coated

with HPMCP, respectively. This study suggests that GTCs, formulated with vitamin C and xylitol followed by γ-CD encapsulation or HPMCP enteric coating, provide combinational effect to increase bioavailability of GTCs.

hero.3350364 REVIEW

Song, Y; Chou, EL; Baecker, A; You, NC; Song, Y; Sun, Q; Liu, S. (2016). Endocrine-disrupting chemicals, risk of type 2 diabetes, and diabetes-related metabolic traits: A systematic review and meta-analysis. J Diabetes 8: 516-532. http://dx.doi.org/10.1111/1753-0407.12325.

BACKGROUND: Elevated blood or urinary concentrations of endocrine-disrupting chemicals (EDCs) may be related to increased risk of type 2 diabetes (T2D). The aim of the present study was to assess the role of EDCs in affecting risk of T2D and related metabolic traits.

METHODS: MEDLINE was searched for cross-sectional and prospective studies published before 8 March 2014 into the association between EDCs (dioxin, polychlorinated biphenyl [PCB], chlorinated pesticide, bisphenol A [BPA], phthalate) and T2D and related metabolic traits. Three investigators independently extracted information on study design, participant characteristics, EDC types and concentrations, and association measures.

RESULTS: Forty-one cross-sectional and eight prospective studies from ethnically diverse populations were included in the analysis. Serum concentrations of dioxins, PCBs, and chlorinated pesticides were significantly associated with T2D risk; comparing the highest to lowest concentration category, the pooled relative risks (RR) were 1.91 (95% confidence interval [CI] 1.44-2.54) for dioxins, 2.39 (95% CI 1.86-3.08) for total PCBs, and 2.30 (95% CI 1.81-2.93) for chlorinated pesticides. Urinary concentrations of BPA and phthalates were also associated with T2D risk; comparing the highest to lowest concentration categories, the pooled RR were 1.45 (95% CI 1.13-1.87) for BPA and 1.48 (95% CI 0.98-2.25) for phthalates. Further, EDC concentrations were associated with indicators of impaired fasting glucose and insulin resistance.

CONCLUSIONS: Persistent and non-persistent EDCs may affect the risk of T2D. There is an urgent need for further investigation of EDCs, especially non-persistent ones, and T2D risk in large prospective studies.

hero.3005706

Spade, DJ; Hall, SJ; Wilson, S; Boekelheide, K. (2015). Di-n-butyl phthalate induces multinucleated germ cells in the rat fetal testis through a non-proliferative mechanism. Biol Reprod 93: 1-15. http://dx.doi.org/10.1095/biolreprod.115.131615.

In utero exposure to some phthalate esters adversely affects the development of the rat seminiferous cord, causing germ cell loss and increasing the number of multinucleated germ cells (MNGs). To understand the timing of MNG formation and determine whether it requires nuclear division, timed pregnant Sprague Dawley rats were exposed to 500 mg/kg di-n-butyl phthalate (DBP) or corn oil vehicle by oral gavage on Gestational Day (GD) 17 or 18 (0 h), and euthanized after 2, 4, 6, or 24 h, or given a second dose at 24 h and euthanized 48 h after the initial dose. Dams were simultaneously exposed to 0.3 M 5-bromo-2'-deoxycitidine (BrdC, converted to BrdU in vivo) through a subcutaneous micro-osmotic pump implanted at -2 h. In the testes of male fetuses, DBP induced MNGs significantly beginning at 4-6 h and dramatically by 24 h when exposure began on GD 18, but not GD 17. Seminiferous cord diameter was significantly elevated in testes of rats treated with DBP at 24 and 48 h, and cell death, measured by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay, was significantly elevated by DBP only at 48 h, when treatment began on GD 18. TUNEL-labeled MNGs were rare. Overall BrdU labeling rate in the testis was unaffected by DBP. Only one of 606 MNGs in BrdU-labeled sections had a strongly positive nucleus, confirming a non-proliferative mechanism of MNG formation, which is a degenerative process with the potential to adversely affect testis development.

hero.3479544

Stacy, SL; Eliot, M; Calafat, AM; Chen, A; Lanphear, BP; Hauser, R; Papandonatos, GD; Sathyanarayana, S; Ye, X; Yolton, K; Braun, JM. (2016). Patterns, Variability, and Predictors of Urinary Bisphenol A Concentrations during Childhood. Environ Sci Technol 50: 5981-5990. http://dx.doi.org/10.1021/acs.est.6b00794.

We examined the patterns, variability, and predictors of urinary bisphenol A (BPA) concentrations in 337 children from the Cincinnati, Ohio HOME Study. From 2003 to 2014, we collected two urine samples from women at 16 and 26 weeks of pregnancy and six urine samples from children at 1-5 and 8 years of age. We

used linear mixed models to calculate intraclass correlation coefficients (ICCs) as a measure of within-person BPA variability and to identify sociodemographic and environmental predictors. For the 8-year visit, we used multivariable linear regression to explore associations between urinary BPA concentrations and exposure-related factors. We calculated daily intakes using equations estimating creatinine excretion rates and creatinine-standardized BPA concentrations. Urinary BPA concentrations, which decreased over childhood, had a low degree of reproducibility (ICC < 0.2). Estimated daily intakes decreased with age and were below the reference dose of 50 µg/kg body weight/day. BPA concentrations were positively associated with consuming food stored or heated in plastic, consuming canned food and beverages, and handling cash register receipts. Our results suggest that there are multiple sources of BPA exposure in young children. Etiological studies should collect serial urine samples to accurately classify BPA exposure and consider sociodemographic and environmental factors as possible confounders.

hero.3070940

Stevenson, M; Alexander, B; Baxter, CS; Leung, YK. (2015). Evaluating Endocrine Disruption Activity of Deposits on Firefighting Gear Using a Sensitive and High Throughput Screening Method. J Occup Environ Med 57: e153-e157. http://dx.doi.org/10.1097/JOM.0000000000000577.

OBJECTIVE: Adverse health outcomes related to exposure to endocrine disrupting chemicals, including increased incidences of coronary heart disease, prostate and testicular cancers, and congenital disabilities, have been reported in firefighters or their offspring. We, therefore, measured the estrogenic and antiestrogenic activity of extracts of used firefighter gear to assess exposure to these agents.

METHODS: Extracts and known chemical contaminants were examined for estrogenicity and antiestrogenicity in yeast cells expressing the estrogen receptor.

RESULTS: Most extracts of used gear and phthalate diesters detectable on this gear displayed strong antiestrogenic effects. Notably, new glove and hood extracts showed significant estrogenic activity.

CONCLUSIONS: Overall, our data suggest that firefighters are exposed to both estrogenic and antiestrogenic agents, possibly phthalates that may lead to health risks observed in this occupation as a result of perturbation of hormone homeostasis.

hero.3469554 REVIEW

Stiel, L; Adkins-Jackson, PB; Clark, P; Mitchell, E; Montgomery, S. (2016). A review of hair product use on breast cancer risk in African American women [Review]. 5: 597-604. http://dx.doi.org/10.1002/cam4.613.

The incidence rate of breast cancer for African American women has recently converged with that of non-Hispanic White women in the United States, although African Americans have a higher mortality rate due to this disease. Although most research exploring health disparities associated with this phenomenon has focused on differences between women based on biology and behavior, both the academic and lay communities have begun to explore the potential role of environmental exposure to estrogen and endocrine disrupting chemicals (EDCs). This study reviews the current state of the science associating one such means of exposure, hair products containing EDCs, with breast cancer risk in African American women. We found a growing body of evidence linking: (1) environmental estrogen and EDC exposures to breast cancer risk, (2) the presence of such chemicals in personal care products, including hair products, and (3) the use of certain hair products with potential breast cancer risk in African Americans. At the same time, there is also increasing concern in the lay community about this risk. These results indicate the need for additional research, and the opportunity to benefit from strategic partnerships in community-collaborative approaches in order to better understand the potential "cost of beauty."

hero.3469283

Sturgeon, SR; Flynn, D; Kaiser, AB; Reeves, KW. (2016). Urinary levels of phthalate metabolites and cardiovascular disease mortality (NHANES, 1999-2008). Int J Hyg Environ Health 219: 876-882. http://dx.doi.org/10.1016/j.ijheh.2016.07.006.

BACKGROUND: Mechanistic data and results from a limited number of cross-sectional epidemiologic studies have suggested a possible link between phthalates and adverse cardiovascular outcomes.

OBJECTIVE: To evaluate the association between urinary levels of eight phthalate metabolites and subsequent risk of cardiovascular death in a prospective cohort analysis.

METHODS: We identified 5080 individuals 40 years or older who participated in

the continuous National Health and Nutrition Examination Survey (NHANES) from 1999 to 2008 and who had measured phthalate levels available. We a priori excluded individuals in later cycles of NHANES with measured phthalates so as to have the potential of at least three years of follow-up time on all members of the cohort. Questionnaire, exam and laboratory data were merged with a public access NHANES mortality file updated through December 31, 2011. The associations between cardiovascular death and quartile levels of the phthalate metabolites were investigated using Cox proportional hazard models.

RESULTS: There were 175 deaths due to cardiovascular disease deaths over a mean of 7.0 years of follow-up. No association between cardiovascular disease mortality and individual urinary phthalate metabolites was observed. After adjustments, hazard ratios comparing the highest to lowest quartile ranged from 0.73 (95%CI: 0.5-1.2) for mono-ethyl phthalate [MEP] to 1.4 (95%CI:0.8-2.5) for mono-(2-ethyl-5-hydroxyhexyl) phthalate [MEHHP].

CONCLUSIONS: Urinary levels of phthalate metabolites were not associated with increased cardiovascular disease mortality. Additional larger cohort studies with longer follow-up focused on cardiovascular disease incidence are needed.

hero.3479560

Su, Y, anHua; Cheng, Q, iJun; Huang, ZX; Zhao, B, in; Chen, JH, ui; Yu, XS; Peng, X, ueQi; Zhao, B, in; Shi, MM; Chen, J; Liu, H, uiFen; Ke, X, iaYi; Zhao, B, enHua; Inc, DP. (2016). Factors Associated with Internal Phthalate Exposure among Pregnant Women. 11-18.

Objective: To analyze the potential factors related to phthalic acid ester (PAE) exposure in pregnant women using multivariate statistical methods. Methods: The study was conducted from April to June 2013 in Xiamen, China. A total of 1020 pregnant women (gestational age <= 16 weeks) met the criteria for inclusion in the cohort. We selected 100 participants by systematic random sampling. Participant information was collected by questionnaires, and urine samples were collected, detect five PAEs (MEP; MBzP; MBP; MEHP; and MMP) levels in urine samples. Single-factor and multi-factor logistic analysis were used to analyze the association between PAE exposure levels and potential associated factors. Results: After creatinine adjustment, medians of the five PAEs in the 100 urine samples were 54.64 mu g/g, 29.25 mu g/g, 17.56 mu g/g, 3.91 mu g/g, and 53.79 mu g/g, respectively. Multivariate analysis results indicated that MMP was associated with education level and the use of hair permanents, hair dyes, and hair dryers; ORs were 0.560 and 2.056, respectively. MEP was associated with education level and makeup use during pregnancy; ORs were 0.548 and 1.968, respectively. MBP was associated with education level, the use of makeup, hair permanents, dyes, and dryers; ORs were 0.559, 1.876, and 2.812, respectively. MBZP was associated with level of education; OR was 0.482. Finally, MEHP was associated with education level, drinking water type, and medication use during pregnancy; ORs were 0.560, 1.972, and 2.100, respectively. Conclusion: PAE exposure levels in pregnant women were associated with level of education, type of drinking water, and use of medication, permanent hair waves, hair dyes, hair dryers or makeup during pregnancy.

hero.3455519

Sun, J; Pan, L; Tsang, DC; Li, Z; Zhu, L; Li, X. (2016). Phthalate esters and organochlorine pesticides in agricultural soils and vegetables from fast-growing regions: a case study from eastern China. Environ Sci Pollut Res. http://dx.doi.org/10.1007/s11356-016-7725-7.

The present study investigated phthalate esters (PAEs) and organochlorine pesticides (OCPs) in agricultural soils and vegetables from eastern China. The concentrations of PAEs ranged from 109 to 5560ng/g in soils and 60.1 to 2390ng/g in cabbages, with average concentrations of 946 and 601ng/g, respectively. The concentrations of OCPs ranged from <0.1 to 662ng/g in soils and <0.1 to 42.8ng/g in cabbages, with average concentrations of 134 and 11.6ng/g, respectively. OCPs were mainly in the 0-30cm surface soil layers, while PAEs could infiltrate in deep soil profiles to 70-80cm layer. Potential source analysis traced the occurrence of OCPs to both historical application and current usage, whereas building materials and agricultural plastic film were possible input sources of PAEs in the ambient environment. OCPs showed no apparent effect on soil microbial communities, whereas significant negative relationship was observed between PAEs and fungi in soils (R=-0.54, p<0.01). Human health risk assessment data revealed marginal noncarcinogenic risks and low carcinogenic risks in these soils. Notably, PAEs posed a comparable or higher risk level compared with that of OCPs. This study suggests the need for better regulation on pollution control and management of PAE-elevated sites to protect soil quality and food safety.

hero.3462441

Sun, J; Pan, L; Tsang, DC; Zhan, Y; Liu, W; Wang, X; Zhu, L; Li, X. (2016). Polychlorinated biphenyls in agricultural soils from the Yangtze River Delta of China: Regional contamination characteristics, combined ecological effects and human health risks. Chemosphere 163: 422-428. http://dx.doi.org/10.1016/j.chemosphere.2016.08.038.
The current contamination status of polychlorinated biphenyls (PCBs) was studied in the agricultural soils of the Yangtze River Delta (YRD), one of the largest economic zones in China. The concentrations of PCBs ranged from <0.1 to 130ng/g dry weight. Higher concentrations of PCBs were observed in the 0-30cm surface layers relative to the subsurface soils. A distinct spatial distribution was observed with a declining concentration gradient from the northwest to the southeast of the region. The composition of PCBs in the soils was consistent with the Chinese commercial PCB mixtures, but different from the compositions in global background soil. Local sources including large-scale use and disposal of PCB-containing products were the main potential sources to soil. The ecological effects and human health risks associated with combined persistent organic pollutants, including PCBs, organochlorine pesticides (OCPs), phthalate esters (PAEs) and polybrominated diphenyl ethers (PBDEs), were further estimated. The four toxic organic compounds and seven physicochemical parameters together could only explain 12.7% of the variation in microbial community composition, suggesting the soil ecosystem function was not strongly influenced by the combined pollution at low concentrations. However, the potential health risks to residents via multiple pathways were notably higher for PCBs than other chemicals. The potential risks were mainly derived from PCB-126, 81, and 169.

hero.3479513 REVIEW

Swaen, GM; Urlings, MJ; Zeegers, MP. (2016). Outcome reporting bias in observational epidemiology studies on phthalates. Ann Epidemiol 26: 597-599.e594. http://dx.doi.org/10.1016/j.annepidem.2016.07.001.

hero.3469468

Tan, W; Zhang, Y; He, X; Xi, B; Gao, R; Mao, X; Huang, C; Zhang, H; Li, D; Liang, Q; Cui, D; Alshawabkeh, AN. (2016). Distribution patterns of phthalic acid esters in soil particle-size fractions determine biouptake in soil-cereal crop systems. Sci Rep 6: 31987. http://dx.doi.org/10.1038/srep31987.
The use of wastewater irrigation for food crops can lead to presence of bioavailable phthalic acid esters (PAEs) in soils, which increase the potential for human exposure and adverse carcinogenic and non-cancer health effects. This study presents the first investigation of the occurrence and distribution of PAEs in a maize-wheat double-cropping system in a wastewater-irrigated area in the North China Plain. PAE levels in maize and wheat were found to be mainly attributed to PAE stores in soil coarse (250-2000 μm) and fine sand (53-250 μm) fractions. Soil particle-size fractions with higher bioavailability (i.e., coarse and fine sands) showed greater influence on PAE congener bioconcentration factors compared to PAE molecular structures for both maize and wheat tissues. More PAEs were allocated to maize and wheat grains with increased soil PAE storages from wastewater irrigation. Additional findings showed that levels of both non-cancer and carcinogenic risk for PAE congeners in wheat were higher than those in maize, suggesting that wheat food security should be prioritized. In conclusion, increased soil PAE concentrations specifically in maize and wheat grains indicate that wastewater irrigation can pose a contamination threat to food resources.

hero.3350295

Tan, Y; Si, X; Zhong, L; Feng, X; Yang, X; Huang, M; Wu, C. (2016). Development and validation of dissolution testings in acidic media for rabeprazole sodium delayed-release capsules. Drug Dev Ind Pharm 42: 1-9. http://dx.doi.org/10.3109/03639045.2016.1161644.
Rabeprazole sodium (RAB) dissolved in acidic media is accompanied by its degradation in the course of dissolution testing. To develop and establish the accumulative release profiles of ACIPHEX() Sprinkle (RAB) delayed-release capsules (ACIPHEX() Sprinkle) in acidic media using USP apparatus 2 (paddle apparatus) as a dissolution tester, the issues of determination of accumulative release amount of RAB in these acidic media and interference of hydroxypropylmethyl cellulose phthalate were solved by adding appropriate hydrochloric acid (HCl) into dissolution samples coupled with centrifugation so as to remove the interference and form a solution of degradation products of RAB, which is of a considerably stable ultraviolet (UV) absorbance at the wavelength of 298 nm within 2.0 h. Therefore, the accumulative release amount of RAB in dissolution samples at each sample time points could be determined by UV-spectrophotometry, and the accumulative

release profiles of ACIPHEX() Sprinkle in the media of pH 1.0, pH 6.0, and pH 6.8 could be established. The method was validated per as the ICH Q2 (R1) guidelines and demonstrated to be adequate for quality control of ACIPHEX() Sprinkle and the accumulative release profiles can be used as a tool to guide the formulation development and quality control of a generic drug for ACIPHEX() Sprinkle.

hero.3479536

Tang, EI; Mruk, DD; Cheng, CY. (2016). Regulation of microtubule (MT)-based cytoskeleton in the seminiferous epithelium during spermatogenesis [Review]. Semin Cell Dev Biol 59: 35-45. http://dx.doi.org/10.1016/j.semcdb.2016.01.004.

In rodents and humans, testicular cells, similar to other mammalian cells, are supported by actin-, microtubule (MT)- and intermediate filament-based cytoskeletons. Although the cytoskeletal network of the testis serves an important role in regulating spermatogenesis during the epithelial cycle, most of the published findings in the literature are limited to studies that only visualize these cytoskeletons in the seminiferous epithelium. Few focus on the underlying molecular mechanism that regulates their organization in the epithelium in response to changes in the stages of the epithelial cycle. Functional studies in the last decade have begun to focus on the role of binding proteins that regulate these cytoskeletons, with some interesting findings rapidly emerging in the field. Since the actin- and intermediate filament-based cytoskeletons have been recently reviewed, herein we focus on the MT-based cytoskeleton for two reasons. First, besides serving as a structural support cytoskeleton, MTs are known to serve as the track to support and facilitate the transport of germ cells, such as preleptotene spermatocytes connected in clones and elongating/elongated spermatids during spermiogenesis, across the blood-testis barrier (BTB) and the adluminal compartment, respectively, during spermatogenesis. While these cellular events are crucial to the completion of spermatogenesis, they have been largely ignored in the past. Second, MT-based cytoskeleton is working in concert with the actin-based cytoskeleton to provide structural support for the transport of intracellular organelles across the cell cytosol, such as endosome-based vesicles, and phagosomes, which contain residual bodies detached from spermatids, to maintain the cellular homeostasis in the seminiferous epithelium. We critically evaluate some recent published findings herein to support a hypothesis regarding the role of MT in conferring germ cell transport in the seminiferous epithelium.

hero.3070976

Tang, F; Tang, Q; Tian, Y; Fan, Q; Huang, Y; Tan, X. (2015). Network pharmacology-based prediction of the active ingredients and potential targets of Mahuang Fuzi Xixin decoction for application to allergic rhinitis. J Ethnopharmacol 176: 402-412. http://dx.doi.org/10.1016/j.jep.2015.10.040.

ETHNOPHARMACOLOGICAL RELEVANCE: Certain herbal formulae from Traditional Chinese Medicine (TCM) are effective for treating and preventing diseases in clinical practice. Mahuang fuzi Xixin Decoction (MFXD) is a TCM that is used to treat allergic rhinitis (AR); however, the active ingredients and potential targets of its action against AR remain unclear. Therefore, further investigation is required.

METHODS: A network pharmacology approach comprising drug-likeness evaluation, oral bioavailability prediction, multiple drug target prediction, and network analysis has been used in this study.

RESULTS: The comprehensive systematic approach was successfully to indentify 41 bioactive ingredients in MFXD, while 37 potential targets hit by these ingredients related to AR. Moreover, wherein four predicted ingredients possess anti-inflammatory effects were found by this technique.

CONCLUSIONS: Our works successfully predict the active ingredients and potential targets of MFXD for application to allergic rhinitis and helps to illustrate mechanism of action on a systematic level. This study not only provides new insights into the chemical basis and pharmacology of MFXD but also demonstrates a feasible method for discovering potential drugs from herbal medicine.

hero.3070970

Thingholm, TE; Larsen, MR. (2016). The Use of Titanium Dioxide for Selective Enrichment of Phosphorylated Peptides. Methods Mol Biol 1355: 135-146. http://dx.doi.org/10.1007/978-1-4939-3049-4_9.

Titanium dioxide (TiO2) has very high affinity for phosphopeptides and in recent years it has become one of the most popular methods for phosphopeptide enrichment from complex biological samples. Peptide loading onto TiO2 resin in a highly acidic environment in the presence of 2,5-dihydroxybenzoic acid (DHB),

phthalic acid, lactic acid, or glycolic acid has been shown to improve selectivity significantly by reducing unspecific binding of non-phosphorylated peptides. The phosphopeptides bound to the TiO2 are subsequently eluted from the chromatographic material using an alkaline buffer. TiO2 chromatography is extremely tolerant towards most buffers used in biological experiments, highly robust and as such it has become the method of choice in large-scale phosphoproteomics. Here we describe a batch mode protocol for phosphopeptide enrichment using TiO2 chromatographic material followed by desalting and concentration of the sample by reversed phase micro-columns prior to downstream MS and LC-MS/MS analysis.

hero.3469242

Thomsen, AM; Riis, AH; Olsen, J; Jönsson, BA; Lindh, CH; Hjollund, NH; Jensen, TK; Bonde, JP; Toft, G. (2017). Female exposure to phthalates and time to pregnancy: a first pregnancy planner study. Hum Reprod 32: 232-238. http://dx.doi.org/10.1093/humrep/dew291.

STUDY QUESTION: Is female exposure to phthalate metabolites associated with reduced fecundity, as estimated by prolonged time to pregnancy (TTP)?

SUMMARY ANSWER: Female exposure to monoethyl phthalate (MEP) but not monobutyl phthalate (MBP), monobenzyl phthalate (MBzP) and monoethylhexyl phthalate (MEHP) was associated with a longer TTP.

WHAT IS KNOWN ALREADY: Male exposure to phthalates is potentially associated with adverse effects on human fecundity in epidemiological studies, but little is known about the potential effects on female reproduction.

STUDY DESIGN SIZE AND DURATION: A cohort study with prospective data based on 229 women from a Danish cohort of 430 first pregnancy planning couples enrolled in 1992-1994. In 2009, urinary analyses of phthalate metabolites were performed on stored urine samples from this cohort.

PARTICIPANTS/MATERIALS, SETTING AND METHODS: We analyzed MEP, MBP, MBzP and MEHP in female morning spot urine samples collected daily during the first 10 days of menstrual cycles after discontinuation of contraception. The exposure assessment was based on the mean of two measurements from each woman collected in a period of 6 menstrual cycles. We used Cox regression with discrete time to estimate fecundability ratios (FRs) and 95% CI in relation to the average urine metabolite concentration exposure level, controlled for age and BMI, and the time-varying variables smoking and alcohol.

MAIN RESULT AND ROLE OF CHANCE: Urinary concentration of MEP was associated with a decreased fecundity (adjusted FR 0.79; 95% CI: 0.63; 0.99) corresponding to a 21% decreased probability of conception for each natural log (ln) unit increase in MEP. No significant association with TTP was found for MBP, MBzP and MEHP.

LIMITATIONS REASONS FOR CAUTION: Subfertile women were overrepresented in the study population due to exclusion of 77 high fertile women who became pregnant in the first cycle when urine collection began.

WIDER IMPLICATIONS OF THE FINDINGS: Our results suggest that female exposure to MEP may have an adverse effect on female fecundity, but these findings need to be replicated in a larger and newer cohort study with sufficient exposure contrast if the use of diethyl phthalate (DEP) and thereby MEP in the future potentially should be regulated in cosmetics and industrial consumer products.

STUDY FUNDING/COMPETING INTERESTS: The original data collected were founded by Aarhus University Research Foundation, the Danish Medical Research Council and the Danish Medical Health Insurance Foundation. There are no conflicts of interest to be declared.

TRIAL REGISTRATION NUMBER: N/A.

hero.3466568

Tran, V; Tindula, G; Huen, K; Bradman, A; Harley, K; Kogut, K; Calafat, AM; Nguyen, B; Parra, K; Ye, X; Eskenazi, B; Holland, N. (2016). Prenatal phthalate exposure and 8-isoprostane among Mexican-American children with high prevalence of obesity. J Dev Orig Health Dis1-10. http://dx.doi.org/10.1017/S2040174416000763.

Oxidative stress has been linked to many obesity-related conditions among children including cardiovascular disease, diabetes mellitus and hypertension. Exposure to environmental chemicals such as phthalates, ubiquitously found in humans, may also generate reactive oxygen species and subsequent oxidative stress. We examined longitudinal changes of 8-isoprostane urinary concentrations, a validated biomarker of oxidative stress, and associations with maternal prenatal urinary concentrations of phthalate metabolites for 258 children at 5, 9 and 14 years of age participating in a birth cohort residing in an agricultural area in California. Phthalates are endocrine disruptors, and in utero exposure has been also linked to altered lipid

metabolism, as well as adverse birth and neurodevelopmental outcomes. We found that median creatinine-corrected 8-isoprostane concentrations remained constant across all age groups and did not differ by sex. Total cholesterol, systolic and diastolic blood pressure were positively associated with 8-isoprostane in 14-year-old children. No associations were observed between 8-isoprostane and body mass index (BMI), BMI Z-score or waist circumference at any age. Concentrations of three metabolites of high molecular weight phthalates measured at 13 weeks of gestation (monobenzyl, monocarboxyoctyl and monocarboxynonyl phthalates) were negatively associated with 8-isoprostane concentrations among 9-year olds. However, at 14 years of age, isoprostane concentrations were positively associated with two other metabolites (mono(2-ethylhexyl) and mono(2-ethyl-5-carboxypentyl) phthalates) measured in early pregnancy. Longitudinal data on 8-isoprostane in this pediatric population with a high prevalence of obesity provides new insight on certain potential cardiometabolic risks of prenatal exposure to phthalates.

hero.3350298

Traore, K; Martinez-Arguelles, DB; Papadopoulos, V; Chen, H; Zirkin, BR. (2016). Repeated exposures of the male Sprague Dawley rat reproductive tract to environmental toxicants: Do earlier exposures to di-(2-ethylhexyl)phthalate (DEHP) alter the effects of later exposures? Reprod Toxicol 61: 136-141. http://dx.doi.org/10.1016/j.reprotox.2016.03.046.

Although exposures to environmental toxicants occur throughout life, little attention has been paid to the possible effects of exposures early in life on later exposure effects. We asked whether DEHP administered in utero (GD14-parturition) affects how male rats respond to later exposures. Neither in utero nor juvenile (PND21-35) exposures to 100mg/kg/day DEHP affected testis weight or histology as assessed on PND35. However, after in utero DEHP, subsequent juvenile exposure resulted in significantly reduced testis weight and altered testicular histology. Both in utero and juvenile exposures resulted in significant reductions in serum testosterone, but there was no effect of earlier on later exposure. Whether or not there had been in utero DEHP exposure, juvenile DEHP exposure had no effect on body, kidney or liver weights. These observations indicate that in utero exposure can, but will not necessarily, alter later exposure effects, with outcomes dependent upon endpoints measured and dose.

hero.3469287

Trasande, L; Lampa, E; Lind, L; Lind, PM. (2016). Population attributable risks and costs of diabetogenic chemical exposures in the elderly. J Epidemiol Commun Health. http://dx.doi.org/10.1136/jech-2016-208006. BACKGROUND: A previous analysis examined the contribution of endocrine disruptor exposures (endocrine-disrupting chemicals, EDCs) to adult diabetes, but was limited to effects of phthalates in middle-aged women and did not simultaneously examine multiple EDCs which are known to coexist in the environment. We therefore endeavoured to quantify potential reductions in diabetes and disease costs that could result from reducing synthetic chemical diabetogenic exposures in the elderly in Europe.

METHODS: We leveraged the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study (1000 participants), which has measured exposure to phthalates; dichlorodiphenyltrichloroethylene; polychlorinated biphenyls (PCBs) and perfluoroalkyl substances to examine their independent contribution to diabetes. We estimated risk reductions assuming identical 25% reductions across levels of 4 selected compounds (PCB 153, monoethylphthalate, dichlorodiphenyldichloroethylene and perfluorononanoic acid), and diabetes costs saved in European men and women if diabetogenic exposures are limited.

RESULTS: Reduction of chemical exposures was associated with a 13% (95% CI 2% to 22%) reduction in prevalent diabetes, compared with 40% resulting from an identical (25%) reduction in body mass index (BMI) in cross-sectional analyses. Extrapolating to Europe, 152 481 cases of diabetes in Europe and 4.51 billion/year in associated costs could be prevented, compared with 469 172 cases prevented by reducing BMI.

CONCLUSIONS: These findings support regulatory and individual efforts to reduce chemical exposures to reduce the burden and costs of diabetes.

hero.3070959

Tsai, CF; Hsieh, TH; Lee, JN; Hsu, CY; Wang, YC; Kuo, KK; Wu, HL; Chiu, CC; Tsai, EM; Kuo, PL. (2015). Curcumin Suppresses Phthalate-Induced Metastasis and the Proportion of Cancer Stem Cell (CSC)-like Cells via the Inhibition of AhR/ERK/SK1 Signaling in Hepatocellular Carcinoma. J Agric Food Chem 63: 10388-10398.

http://dx.doi.org/10.1021/acs.jafc.5b04415.
Recent evidence indicating that phthalates promote cancer development, including cell proliferation, migration, and invasion, has raised public health concerns. Here, we show that bis(2-ethylhexyl) phthalate promotes the migration, invasion, and epithelial-mesenchymal transition of hepatocellular carcinoma cells. In addition, bis(2-ethylhexyl) phthalate increased the proportion of cancer stem cell (CSC)-like cells and stemness maintenance in vitro as well as tumor growth and metastasis in vivo. The various activities of curcumin, including anticancer, anti-inflammation, antioxidation, and immunomodulation, have been investigated extensively. Curcumin suppressed phthalate-induced cell migration, invasion, and epithelial-mesenchymal transition, decreased the proportion of CSC-like cells in hepatocellular carcinoma cell lines in vitro, and inhibited tumor growth and metastasis in vivo. We also reveal that curcumin suppressed phthalate-induced migration, invasion, and CSC-like cell maintenance through inhibition of the aryl hydrocarbon receptor/ERK/SK1/S1P3 signaling pathway. Our results suggest that curcumin may be a potential antidote for phthalate-induced cancer progression.

hero.3469519

Tsai, HJ; Wu, CF; Tsai, YC; Huang, PC; Chen, ML; Wang, SL; Chen, BH; Chen, CC; Wu, WC; Hsu, PS; Hsiung, CA; Wu, MT. (2016). Intake of Phthalate-tainted Foods and Serum Thyroid Hormones in Taiwanese Children and Adolescents. Sci Rep 6: 30589. http://dx.doi.org/10.1038/srep30589.
On April-May, 2011, phthalates, mainly Di-(2-ethylhexyl) phthalate (DEHP), were deliberately added to a variety of foodstuff as a substitute emulsifier in Taiwan. This study investigated the relationship between DEHP-tainted foodstuffs exposure and thyroid function in possibly affected children and adolescents. Two hundred fifty participants <18 years possibly exposed to DEHP were enrolled in this study between August 2012 and January 2013. Questionnaires were used to collect details on their past exposure to DEHP-tainted food items. Blood and urine samples were collected for biochemical workups to measure current exposure derived from three urinary DEHP metabolites using a creatinine excretion-based model. More than half of 250 participants were estimated to be exposed to DEHP-tainted foods found to exceed the recommend tolerable daily intake of DEHP established by the European Food Safety Authority (<50 μg/kg/day). The median daily DEHP intake (DDI) among those 250 participants was 46.52 μg/kg/day after multiple imputation. This value was ~10-fold higher than the current median DEHP intake (4.46 μg/kg/day, n = 240). Neither past nor current DEHP exposure intensity was significantly associated with serum thyroid profiles. Future studies may want to follow the long-term health effects of this food scandal in affected children and adolescents.

hero.3466579

Tsochatzis, ED; Tzimou-Tsitouridou, R; Gika, HG. (2016). Analytical methodologies for the assessment of phthalate exposure in humans. Crit Rev Anal Chem0. http://dx.doi.org/10.1080/10408347.2016.1273754.
Screening and quantification of phthalate metabolites in biological matrices provides information on the phthalate exposure. The preferred tool for the determination of phthalate metabolites is liquid chromatography-mass spectrometry, typically preceded by a sample extraction step. Method development for the determination of phthalate metabolites by hyphenated techniques faces challenges due to the widespread occurrence of phthalates in the laboratory and sample collection materials which impairs their accurate quantification. Here the analytical methods that have been developed for the determination of biomarkers of phthalates in various matrices are presented, and limitations and challenges in these applications are discussed.

hero.3469445

Varshavsky, JR; Zota, AR; Woodruff, TJ. (2016). A Novel Method for Calculating Potency-Weighted Cumulative Phthalates Exposure with Implications for Identifying Racial/Ethnic Disparities among U.S. Reproductive-Aged Women in NHANES 2001-2012. Environ Sci Technol 50: 10616-10624. http://dx.doi.org/10.1021/acs.est.6b00522.
Phthalates are ubiquitous chemicals linked to hormonal disruptions that affect reproduction and development. Multiple antiandrogenic phthalates exposure during fetal development can have greater impacts than individual exposure; thus, the National Academy of Sciences (NAS) recommends them for cumulative assessment. Using National Health and Nutrition Examination Survey data (NHANES, 2001-2012),

we developed a potency-weighted sum of daily intake (androgen-disruptor; µg/kg/day) of di-n-butyl phthalate (DnBP), diisobutyl phthalate (DiBP), butyl benzyl phthalate (BBzP), and di(2-ethylhexyl) phthalate (DEHP) based on NAS recommendations, and included diethyl phthalate (DEP) and diisononyl phthalate (DiNP) in additional metrics (2005-2012). We compared racial/ethnic differences in androgen-disruptor among 2842 reproductive-aged women. In sensitivity analyses, we assessed the influence of potency assumptions, alternate urine dilution adjustment methods, and weighting phthalate metabolites directly rather than daily intake estimates of parent compounds. We found that DEHP contributed most to androgen-disruptor (48-64%), and that androgen-disruptor decreased over time. Black women generally had higher cumulative exposures than white women, although the magnitude and precision of the difference varied by model specification. Our approach provides a blueprint for combining chemical exposures linked to common adverse outcomes, and should be considered in future exposure, risk, and epidemiological studies.

hero.3479510

Vidal, RB; Ibañez, GA; Escandar, GM. (2016). A green method for the quantification of plastics-derived endocrine disruptors in beverages by chemometrics-assisted liquid chromatography with simultaneous diode array and fluorescent detection. Talanta 159: 336-343. http://dx.doi.org/10.1016/j.talanta.2016.06.049.

The aim of this study was to develop a novel analytical method for the determination of bisphenol A, nonylphenol, octylphenol, diethyl phthalate, dibutyl phthalate and diethylhexyl phthalate, compounds known for their endocrine-disruptor properties, based on liquid chromatography with simultaneous diode array and fluorescent detection. Following the principles of green analytical chemistry, solvent consumption and chromatographic run time were minimized. To deal with the resulting incomplete resolution in the chromatograms, a second-order calibration was proposed. Second-order data (elution time-absorbance wavelength and elution time-fluorescence emission wavelength matrices) were obtained and processed by multivariate curve resolution-alternating least-squares (MCR-ALS). Applying MCR-ALS allowed quantification of the analytes even in the presence of partially overlapped chromatographic and spectral bands among these compounds and the potential interferents. The obtained results from the analysis of beer, wine, soda, juice, water and distilled beverage samples were compared with gas chromatography-mass spectrometry (GC-MS). Limits of detection (LODs) in the range 0.04-0.38ngmL(-1) were estimated in real samples after a very simple solid-phase extraction. All the samples were found to contain at least three EDs, in concentrations as high as 334ngmL(-1).

hero.3469361

Wada, K; de Vrijer, B; Hales, BF; Nisker, J. (2016). Implications of Applying Minimal Risk Standards in Clinical Research to Information Provision in Prenatal and Pre-conception Care. J Obstet Gynaecol Can 38: 965-974. http://dx.doi.org/10.1016/j.jogc.2016.05.007.

BACKGROUND: There have long been minimal risk thresholds beneath which risks may not need to be discussed in clinical research. This threshold concept may be applied to clinical practice. Our research explored application of minimal risk standards in research regulations to providing information in prenatal and pre-conception care.

METHODS: A case study approach applied minimal risk standards in research regulations to prenatal and pre-conception care with respect to the risks of excess alcohol consumption, folic acid insufficiency, exposure to phthalate plasticizers, and exposure to brominated flame retardants (BFRs).

RESULTS: Excess alcohol consumption and folic acid insufficiency were found to be above the minimal risk standards as outlined in research regulations, while exposure to phthalates and BFRs requires more evidence to determine whether they are above minimal risk. However, applying the minimal risk standard based on the daily life of a healthy adult or a fetus in a healthy pregnant woman, phthalates and BFRs are at the minimal risk threshold regardless of their potential harm since all pregnant women may be exposed to these chemicals in their daily life. Nevertheless, if there is demonstration of sufficient evidence of harm, they may be above minimal risk if such harm can be reduced by individual choice to avoid exposure.

CONCLUSION: The minimal risk concept in research regulations as applied to clinical practice may be useful to help clinicians and professional organizations determine what risks need be discussed in prenatal and pre-conception care.

hero.3469535

Wallner, P; Kundi, M; Hohenblum, P; Scharf, S; Hutter, HP. (2016). Phthalate Metabolites, Consumer Habits and Health Effects. Int J Environ Res Public Health 13. http://dx.doi.org/10.3390/ijerph13070717.

Phthalates are multifunctional chemicals used in a wide variety of consumer products. The aim of this study was to investigate whether levels of urinary phthalate metabolites in urine samples of Austrian mothers and their children were associated with consumer habits and health indicators. Within an Austrian biomonitoring survey, urine samples from 50 mother-child pairs of five communities (two-stage random stratified sampling) were analysed. The concentrations of 14 phthalate metabolites were determined, and a questionnaire was administered. Monoethyl phthalate (MEP), mono-n-butyl phthalate (MnBP), mono-isobutyl phthalate (MiBP), monobenzyl phthalate (MBzP), mono-(2-ethylhexyl) phthalate (MEHP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (5OH-MEHP), mono-(2-ethyl-5-oxohexyl) phthalate (5oxo-MEHP), mono-(5-carboxy-2-ethylpentyl) phthalate (5cx-MEPP), and 3-carboxy-mono-propyl phthalate (3cx-MPP) could be quantified in the majority of samples. Significant correlations were found between the use of hair mousse, hair dye, makeup, chewing gum, polyethylene terephthalate (PET) bottles and the diethyl phthalate (DEP) metabolite MEP. With regard to health effects, significant associations of MEP in urine with headache, repeated coughing, diarrhoea, and hormonal problems were observed. MBzP was associated with repeated coughing and MEHP was associated with itching.

hero.3468517

Wang, A; Padula, A; Sirota, M; Woodruff, TJ. (2016). Environmental influences on reproductive health: the importance of chemical exposures [Review]. Fertil Steril 106: 905-929. http://dx.doi.org/10.1016/j.fertnstert.2016.07.1076.

Chemical exposures during pregnancy can have a profound and life-long impact on human health. Because of the omnipresence of chemicals in our daily life, there is continuous contact with chemicals in food, water, air, and consumer products. Consequently, human biomonitoring studies show that pregnant women around the globe are exposed to a variety of chemicals. In this review we provide a summary of current data on maternal and fetal exposure, as well as health consequences from these exposures. We review several chemical classes, including polychlorinated biphenyls, perfluoroalkyl substances, polybrominated diphenyl ethers, phenols, phthalates, pesticides, and metals. Additionally, we discuss environmental disparities and vulnerable populations, and future research directions. We conclude by providing some recommendations for prevention of chemical exposure and its adverse reproductive health consequences.

hero.3479516

Wang, H; Gao, M; Gao, J; Yu, N; Huang, H; Yu, Q; Wang, X. (2016). Determination of fluoroquinolone antibiotics via ionic-liquid-based, salt-induced, dual microextraction in swine feed. Anal Bioanal Chem 408: 6105-6114. http://dx.doi.org/10.1007/s00216-016-9719-1.

In conventional microextraction procedures, the disperser (organic solvent or ionic liquid) is left in the aqueous phase and discarded after finishing the microextraction process. Because the disperser is water-soluble, it results in low extraction recovery for polar compounds. In this investigation, an ionic-liquid-based microextraction (ILBME) was integrated with salting-out assisted liquid-liquid microextraction (SALLME) to build an ionic-liquid-based, salt-induced, dual microextraction (ILSDME) for isolation of five fluoroquinolone antibiotics (FQs) with high polarity (log P, -1.0 to 1.0). The proposed ILSDME method incorporates a dual microextraction by converting the disperser in the ILBME to the extractor in the SALLME. Optimization of key factors was conducted by integrating single-factor experiments and central composite design. The optimized experimental parameters were 80μL [C8MIM][PF6] as extractor, 505μL acetone as disperser, pH = 2.0, 4.1min extraction time, and 4.2g of Na2SO4. Under optimized conditions, high ERs (90.6-103.2%) and low LODs (0.07-0.61μgkg(-1)) were determined for five FQs in swine feed. Experimental precision based on RSDs was 1.4-5.2% for intra-day and 2.4-6.9% for inter-day analyses. The combination of ILBME with SALLME increased FQ recoveries by 15-20% as compared with SALLME, demonstrating that the ILSDME method can enhance extraction efficiency for polar compounds compared to single-step microextraction. Therefore, the ILSDME method developed in this study has wide application for pretreatment of moderately to highly polar pollutants in complex matrices. Graphical Abstract A dual microextraction was developed by integrating ionic-liquid-based microextraction with salting-out assisted liquid-liquid microextraction for isolation of five fluoroquinolone antibiotics (FQs) with high polarity (log P = -1.0 to 1.0). The principle of dual microextraction is based on converting the remaining disperser from the first microextraction into an extractor in the second

microextraction. Single-factor experiment and central composite design were applied for optimizing operational parameters using 3D response surfaces and contour lines. Under optimized conditions, the method provided high extraction recoveries and low LODs for five FQs in swine feed. The prominent advantage of the dual microextraction is rapid and highly efficient extraction of moderately to highly polar fluoroquinolones from complex matrices.

hero.3479554

Wang, H; Hu, L; Li, W; Yang, X; Lu, R; Zhang, S; Zhou, W; Gao, H; Li, J. (2017). In-syringe dispersive liquid-liquid microextraction based on the solidification of ionic liquids for the determination of benzoylurea insecticides in water and tea beverage samples. Talanta 162: 625-633. http://dx.doi.org/10.1016/j.talanta.2016.10.035.

A novel in-syringe dispersive liquid-liquid microextraction based on the solidification of ionic liquids (in-syringe SIL-DLLME) was coupled with high-performance liquid chromatography-ultraviolet detector (HPLC-UVD) to detect five benzoylurea insecticides (BUs) in water and tea beverage samples. In this method, the hydrophobic ionic liquid [N8881][PF6] was formed in situ by the metathesis reaction between [N8881]Cl and the anion-exchange reagent KPF6 to extract the target analytes. The whole extraction procedure was performed in a syringe. The solidified extractant could be separated from the aqueous phase by exposing the emulsified extraction solution to an ice bath and then easily collected by squeezing out the aqueous phase through the prepared NWPP-based needle. Various parameters affecting the extraction efficiency, such as the amount of [N8881]Cl, the molar ratio of [N8881]Cl to KPF6, salt addition, cooling time, solution temperature, sample pH and sample volume, were evaluated. Under the optimized conditions, the proposed method was validated with satisfactory results: good linearities with coefficients of determination greater than 0.99 were obtained in the range of 2-500μgL(-1); the limits of detection varied between 0.29 and 0.59μgL(-1); the recoveries of the five benzoylurea insecticides ranged from 85.93% to 90.52%; and the intra-day (n=3) and inter-day (n=3) relative standard deviations were less than 5.36%. Finally, the proposed method was successfully used for the determination of BUs in real water and tea beverage samples.

hero.3071013

Wang, J; Zhang, L; Xin, D; Yang, Y. (2015). Dispersive Micro-Solid-Phase Extraction Based on Decanoic Acid Coated-Fe3 O4 Nanoparticles for HPLC Analysis of Phthalate Esters in Liquor Samples. J Food Sci 80: C2452-C2458. http://dx.doi.org/10.1111/1750-3841.13101.

A novel, simple and low cost through coating Fe3 O4 magnetic nanoparticles (MNPs) with decanoic acid were synthesized. The functionalized MNPs showed excellent dispersibility in aqueous solution and were applied to dispersive micro-solid-phase extraction(D-μ-SPE) followed by high performance liquid chromatographic analysis for 4 phthalate esters (PAEs) including benzyl butyl phthalate (BBP), dicyclohexyl phthalate (DCHP), di-n-butyl phthalate (DBP), and di-n-octyl phthalate (DNOP) from liquor samples. The extraction equilibrium is achieved in 1 min. The MNPs allow easy and rapid isolation of PAEs by using an external magnet, which can be reused 5 times. The 4 PAEs linear dynamic ranges were in the range of 5 to 1000 ng/mL and the correlation coefficients values were 0.9999. The limits of detection were in the range of 0.91 to 2.43 ng/mL. The influences of the adsorbent dosage and the use frequency of adsorbent, the adsorption time, the solution pH and ionic strength were investigated and optimized. The proposed method was used to determine of PAEs in liquor samples and recoveries between 88.9% and 105.4%, with the relative standard deviations were below 4.0%.

hero.3355406

Wang, L; Zhang, W; Tao, W; Wang, L; Shi, X; Lu, X. (2016). Investigating into composition, distribution, sources and health risk of phthalic acid esters in street dust of Xi'an City, Northwest China. Environ Geochem Health. http://dx.doi.org/10.1007/s10653-016-9856-7.

Phthalic acid esters (PAEs) are widely used as plasticizers and in consumer products, which may enter the environment and present risks to human health. U.S. EPA classifies six PAEs as priority pollutants, which could be accumulated in street dust at the interface of atmosphere, biosphere and geosphere. This study collected a total of 58 street dust samples from Xi'an City in Northwest China and analyzed for concentrations of the priority PAEs. Composition, distribution, sources and health risk of the PAEs were further examined. All the priority PAEs were detected in the street dust. The concentrations of individual PAEs varied between not detected and 183.19mg/kg. The sum of the 6 priority PAEs (6PAEs) ranged from

0.87 to 250.30mg/kg with a mean of 40.48mg/kg. The most abundant PAEs in the street dust were di-n-butyl phthalate and di (2-ethylhexyl) phthalate (DEHP). Higher concentrations of 6PAEs in the street dust were found in the south and west parts of Xi'an City as well as its urban center, which were possibly attributed to the prevailing northerly Asian winter monsoon. The PAEs in the street dust originated mainly from wide application of plasticizers as well as cosmetics and personal care products. The main pathways of human exposure to PAEs in the street dust were ingestion and dermal adsorption of dust particles. The non-cancer risk of human exposure to PAEs in the street dust was relatively low, while the risk to children was higher than that to adults. The cancer risk of human exposure to DEHP in the street dust was lower than the standard limit value of 10(-6).

hero.3070971

Wang, X; Song, M; Guo, M; Chi, C; Mo, F; Shen, X. (2015). Pollution levels and characteristics of phthalate esters in indoor air in hospitals. J Environ Sci 37: 67-74. http://dx.doi.org/10.1016/j.jes.2015.02.016.

The concentrations of phthalate esters (PAEs) in Chinese hospitals were investigated by simultaneously determining concentrations of gas- and particle-phase PAEs. PAEs were detected in two third-class first-grade hospitals, two second-class first-grade hospitals, and a community health service center. Hospital drugstores had the highest concentration (24.19μg/m(3)), which was 1.54 times that of newly decorated houses. The second highest concentration was found in the transfusion rooms, averaging 21.89μg/m(3); this was followed by the concentrations of PAEs in the nurse's workstations, the wards, and the doctor's offices, with mean concentrations of 20.66, 20.0, and 16.92μg/m(3), respectively. The lowest concentrations were found in the hallways (16.30μg/m(3)). Of the six different kinds of PAEs found, major pollutants included diethyl phthalates, dibutyl phthalates, butylbenzyl phthalates and di(2-ethylhexyl) phthalates, comprising more than 80% of all PAEs present. Meanwhile, a comparison between different wards showed that PAE concentrations in the maternity wards were 1.63 times higher than in the main wards. Based on known health hazards, our results suggest that the PAEs seriously influence the health of the pregnant women and babies; therefore, it is of great importance to take the phthalate concentrations in hospitals into consideration. In addition, hospital indoor air was more seriously contaminated than the air of newly decorated houses.

hero.3479556 REVIEW

Wang, Y; Hollis-Hansen, K; Ren, X; Qiu, Y; Qu, W. (2016). Do environmental pollutants increase obesity risk in humans? [Review]. 17: 1179-1197. http://dx.doi.org/10.1111/obr.12463.

OBJECTIVES: Obesity has become a global epidemic and threat to public health. A good understanding of the causes can help attenuate the risk and spread. Environmental pollutants may have contributed to the rising global obesity rates. Some research reported associations between chemical pollutants and obesity, but findings are mixed. This study systematically examined associations between chemical pollutants and obesity in human subjects.

METHODS: Systematic review of relevant studies published between 1 January 1995 and 1 June 2016 by searching PubMed and MEDLINE.

RESULTS: Thirty-five cross-sectional (n = 17) and cohort studies (n = 18) were identified that reported on associations between pollutants and obesity measures. Of them, 16 studies (45.71%) reported a positive association; none reported a sole inverse association; three (8.57%) reported a null association only; six (17.14%) reported both a positive and null association; seven (20.00%) reported a positive and inverse association; and three studies (8.57%) reported all associations (positive, inverse and null). Most studies examined the association between multiple different pollutants, different levels of concentration and in subsamples, which results in mixed results. Thirty-three studies reported at least one positive association between obesity and chemicals, such as polychlorinated biphenyls, biphenyl A, dichlorodiphenyltrichloroethane, dichlorodiphenyldichloroethylene and more. Certain chemicals, such as biphenyl A, were more likely to have high ORs ranging from 1.0 to 3.0, whereas highly chlorinated polychlorinated biphenyls were more likely to have negative ORs. Effects of chemicals on the endocrine system and obesity might vary by substance, exposure level, measure of adiposity and subject characteristics (e.g. sex and age).

CONCLUSIONS: Accumulated evidences show positive associations between pollutants and obesity in humans. Future large, long-term, follow-up studies are needed to assess impact of chemical pollutants on obesity risk and related mechanisms.

hero.3469506

Wang, Y; Yang, Q; Liu, W; Yu, M; Zhang, Z; Cui, X. (2016). DEHP exposure in utero disturbs sex determination and is potentially linked with precocious puberty in female mice. Toxicol Appl Pharmacol 307: 123-129. http://dx.doi.org/10.1016/j.taap.2016.08.001.

Human's ubiquitous exposure to di (2-ethylhexyl) phthalate (DEHP) is thought to be associated with female reproductive toxicity. Previous studies found that DEHP inhibited follicle growth and decreased estradiol levels in adult female mice. However, limited information is available on the link between in utero DEHP exposure and ovarian development in female mouse offspring. The present study evaluates the disturbances in regulatory genes involved in female sex determination and the ovarian outcomes in fetal and postnatal female mice treated with in utero DEHP exposure. Pregnant mice were exposed to DEHP by gavage, with the dosage regime beginning at human relevant exposure levels. After in utero DEHP exposure, increased follicular atresia was observed in the female pups at postnatal days (PND) 21. Foxl2 expression was significantly upregulated, and Fst was significantly downregulated by DEHP above 2mg/kg/d at PND 1 and 21. This suggests that lesion of granulosa cell differentiation and disturbance of follicle development in postnatal female mice. The expression of Cyp11a1 and Star were significantly downregulated by in utero DEHP exposure, indicating effects on estradiol biosynthesis. The female sex determination pathway was disturbed in fetus by DEHP at 2mg/kg/d and above during the critical time window of sex determination causing significant upregulation of Foxl2, Wnt4, β-catenin and Fst. Furthermore, the increased expression of Wnt4 was supported by whole-mount in situ hybridization (WISH). These results suggest a possible association between in utero DEHP exposure and precocious puberty in the postnatal life of mice offspring, where disturbance of the sex determination regulating pathway acted as an important mechanism.

hero.3350206

Watkins, DJ; Milewski, S; Domino, SE; Meeker, JD; Padmanabhan, V. (2016). Maternal phthalate exposure during early pregnancy and at delivery in relation to gestational age and size at birth: A preliminary analysis. Reprod Toxicol 65: 59-66. http://dx.doi.org/10.1016/j.reprotox.2016.06.021.

Epidemiologic studies of in utero phthalate exposure and birth outcomes have had conflicting findings. The objective of this study was to characterize maternal phthalate exposure across pregnancy, examine associations between maternal phthalate levels and infant size and gestational age at birth, and investigate relationships between concurrent bisphenol A (BPA) and phthalate exposure and birth outcomes. Women in the Michigan Mother-Infant Pairs cohort provided urine and blood samples during their first trimester and at delivery. Urinary phthalate metabolites and serum BPA were measured at both time points, and birth weight, length, head circumference, and gestational age were recorded from medical records. Maternal DEHP metabolite concentrations were significantly higher at delivery compared to the first trimester (p<0.05), suggesting increased DEHP exposure late in pregnancy. A number of phthalate metabolites were associated with birth size and gestational age in patterns that varied by sex and timing of exposure, independent of BPA exposure.

hero.3454652

Wei, W; Mandin, C; Blanchard, O; Mercier, F; Pelletier, M; Le Bot, B; Glorennec, P; Ramalho, O. (2017). Predicting the gas-phase concentration of semi-volatile organic compounds from airborne particles: Application to a French nationwide survey. Sci Total Environ 576: 319-325. http://dx.doi.org/10.1016/j.scitotenv.2016.10.074.

Semi-volatile organic compounds (SVOCs) partition indoors between the gas phase, airborne particles, settled dust, and other surfaces. Unknown concentrations of SVOCs in the gas phase (Cg) can be predicted from their measured concentrations in airborne particles. In previous studies, the prediction of Cg depended largely on choosing a specific equation for the calculation of the particle/gas partition coefficient. Moreover, the prediction of Cg is frequently performed at a reference temperature rather than the real indoor temperature. In this paper, a probabilistic approach based on Monte Carlo simulation was developed to predict the distribution of SVOCs' Cg from their concentrations in airborne particles at the target indoor temperature. Moreover, the distribution of the particle/gas partition coefficient of each SVOC at the target temperature was used. The approach was validated using two measured datasets in the literature: the predicted Cg from concentrations measured in airborne particles and the measured Cg were generally of the same order of magnitude. The distributions of the Cg of 66 SVOCs in the French housing stock were then predicted. The SVOCs with the highest median Cg, ranging from 1ng/m(3) to >100ng/m(3), included 8

phthalates (DEP, DiBP, DBP, DEHP, BBP, DMP, DiNP, and DMEP), 4 polycyclic aromatic hydrocarbons (fluorene, phenanthrene, fluoranthene, and anthracene), 2 alkylphenols (4-tert-butylphenol and 4-tert-octylphenol), 2 synthetic musks (galaxolide and tonalide), tributyl phosphate, and heptachlor. The nationwide, representative, predicted Cg values of SVOCs are frequently of the same order of magnitude in Europe and North America, whereas these Cg values in Chinese and Indian dwellings and the Cg of polybrominated diphenyl ethers in U.S. dwellings are generally higher.

hero.3350269

Williams, KE; Lemieux, GA; Hassis, ME; Olshen, AB; Fisher, SJ; Werb, Z. (2016). Quantitative proteomic analyses of mammary organoids reveals distinct signatures after exposure to environmental chemicals. Proc Natl Acad Sci USA 113: E1343-E1351. http://dx.doi.org/10.1073/pnas.1600645113.

Common environmental contaminants such as bisphenols and phthalates and persistent contaminants such as polychlorinated biphenyls are thought to influence tissue homeostasis and carcinogenesis by acting as disrupters of endocrine function. In this study we investigated the direct effects of exposure to bisphenol A (BPA), mono-n-butyl phthalate (Pht), and polychlorinated biphenyl 153 (PCB153) on the proteome of primary organotypic cultures of the mouse mammary gland. At low-nanomolar doses each of these agents induced distinct effects on the proteomes of these cultures. Although BPA treatment produced effects that were similar to those induced by estradiol, there were some notable differences, including a reduction in the abundance of retinoblastoma-associated protein and increases in the Rho GTPases Ras-related C3 botulinum toxin substrate 1 (Rac1) and cell division cycle protein CDC42. Both Pht and PCB153 induced changes that were distinct from those induced by estrogen, including decreased levels of the transcriptional corepressor C-terminal binding protein 1. Interestingly, the three chemicals appeared to alter the abundance of distinct splice forms of many proteins as well as the abundance of several proteins that regulate RNA splicing. Our combined results indicate that the three classes of chemical have distinct effects on the proteome of normal mouse mammary cultures, some estrogen-like but most estrogen independent, that influence diverse biological processes including apoptosis, cell adhesion, and proliferation.

hero.3469243

Wolff, MS; Pajak, A; Pinney, SM; Windham, GC; Galvez, M; Rybak, M; Silva, MJ; Ye, X; Calafat, AM; Kushi, LH; Biro, FM; Teitelbaum, SL; Program, BCaER. (2016). Associations of urinary phthalate and phenol biomarkers with menarche in a multiethnic cohort of young girls. Reprod Toxicol 67: 56-64. http://dx.doi.org/10.1016/j.reprotox.2016.11.009.

To study potential environmental influences on puberty in girls, we investigated urinary biomarkers in relation to age at menarche. Phenols and phthalates were measured at baseline (6-8 years of age). Menarche was ascertained over 11 years for 1051 girls with menarche and biomarkers. Hazards ratios were estimated from Cox models adjusted for race/ethnicity and caregiver education (aHR, 95% confidence intervals [CI] for 5th vs 1st quintile urinary biomarker concentrations). 2,5-Dichlorophenol was associated with earlier menarche (aHR 1.34 [1.06-1.71]); enterolactone was associated with later menarche (aHR 0.82 [0.66-1.03]), as was mono-3-carboxypropyl phthalate (MCPP) (aHR 0.73 [0.59-0.91]); the three p-trends were <0.05. Menarche differed by 4-7 months across this range. Enterolactone and MCPP associations were stronger in girls with below-median body mass index. These analytes were also associated with age at breast development in this cohort. Findings from this prospective study suggest that some childhood exposures are associated with pubertal timing.

hero.3071071

Wood, RK; Crowley, E; Martyniuk, CJ. (2015). Developmental profiles and expression of the DNA methyltransferase genes in the fathead minnow (Pimephales promelas) following exposure to di-2-ethylhexyl phthalate. Fish Physiol Biochem 42: 7-18. http://dx.doi.org/10.1007/s10695-015-0112-3.

DNA methylation is an epigenetic regulator of gene expression, and this process has been shown to be disrupted by environmental contaminants. Di-2-(ethylhexyl) phthalate (DEHP) and related phthalate esters have been shown to affect development in early life stages of fish and can alter genomic methylation patterns in vertebrates. The objectives of this study were the following: (1) Describe the expression patterns of the DNA methyltransferase (dnmt) genes during early fathead minnow (FHM) development. These genes are critical for methylation and imprinting during development. (2) Determine the effects of DEHP on the

development of FHM larvae [1 and 14days post-hatch (dph)]. (3) Determine the effect of DEHP on dnmt expression and global methylation status in larval FHM. FHMs were first collected over a developmental time course [1, 3, 5, 6, and 14days post-fertilization (dpf)] to investigate the expression patterns of five dnmt isoforms. The expression of dnmt1 and dnmt7 was relatively high in embryos at 1 dpf but was variable in expression, and these transcripts were later expressed at a lower level (>3 dpf); dnmt3 was significantly higher in embryos at 1 dpf compared to those at 3 dpf. Dnmt6 showed more of a constitutive pattern of expression during the first 2weeks of development, and the mRNA levels of dnmt8 were higher in embryos at 5 and 6 dpf compared to those at 1 and 3 dpf, corresponding to the hatching period of the embryos. A waterborne exposure to three concentrations of DEHP (1, 10 and 100μg/L) was conducted on 1-day FHM embryos for 24h and on larval fish for 2weeks, ending at 14 dpf. DEHP did not negatively affect survival, hatch rate, or the expression of dnmt isoforms in FHMs. There were no differences in global cytosine methylation following DEHP treatments in 14 dpf larvae, suggesting that environmentally relevant levels of DEHP may not affect global methylation at this stage of FHMdevelopment. However, additional targeted methylome studies are required to determine whether specific gene promoters are differently methylated following exposure to DEHP. This study offers new insight into the roles of the dnmt enzymes during FHM development.

hero.3466589

Wu, H; Ashcraft, L; Whitcomb, BW; Rahil, T; Tougias, E; Sites, CK; Pilsner, JR. (2017). Parental contributions to early embryo development: influences of urinary phthalate and phthalate alternatives among couples undergoing IVF treatment. Hum Reprod 32: 65-75. http://dx.doi.org/10.1093/humrep/dew301.

STUDY QUESTION: Are preconception urinary concentrations of phthalates and phthalate alternatives associated with diminished early stage embryo quality in couples undergoing IVF?

SUMMARY ANSWER: Male, but not female, urinary concentrations of select metabolites of phthalates and phthalate alternatives are associated with diminished blastocyst quality.

WHAT IS KNOWN ALREADY: Although phthalates are endocrine disrupting compounds associated with adverse reproductive health, they are in widespread use across the world. Male and female preconception exposures to select phthalates have been previously associated with adverse reproductive outcomes in both the general population and in those undergoing IVF.

STUDY DESIGN, SIZE, DURATION: This prospective cohort included 50 subfertile couples undergoing IVF in western Massachusetts.

PARTICIPANTS/MATERIALS, SETTING, METHODS: This study includes the first 50 couples recruited from the Baystate Medical Center's Fertility Center in Springfield, MA, as part of the Sperm Environmental Epigenetics and Development Study (SEEDS). Relevant data from both partners, including embryo quality at the cleavage (Day 3) and blastocyst (Day 5) stages, were collected by clinic personnel during the normal course of an IVF cycle. A spot urine sample was collected from both male and female partners on the same day as semen sample procurement and oocyte retrieval. Concentrations of 17 urinary metabolite were quantified by liquid chromatography mass spectrometry and normalized via specific gravity. Generalized estimating equations were used to estimate odds ratios (OR) and 95% CI, with urinary phthalates and phthalate alternatives fitted as continuous variables and embryo quality as a binary variable.

MAIN RESULTS AND THE ROLE OF CHANCE: The 50 couples contributed 761 oocytes, of which 423 progressed to the cleavage stage, 261 were high-quality cleavage stage embryos, 137 were transferrable quality blastocysts and 47 were high-quality blastocysts. At the cleavage stage, male urinary monoethyl phthalate concentrations were positively associated with high-quality cleavage stage embryos (OR = 1.20, 95% CI 1.01-1.43, P = 0.04); no other significant associations were observed at this stage. At the blastocyst stage, male urinary concentrations of monobenzyl phthalate (OR = 0.55, 95% CI 0.36-0.84, P = 0.01), mono-3-hydroxybutyl phthalate (OR = 0.37, 95% CI 0.18-0.76, P = 0.01), mono-n-butyl phthalate (OR = 0.55, 95% CI 0.42-0.73, P < 0.01) and monomethyl phthalate (OR = 0.39, 95% CI 0.26-0.60, P < 0.01) were inversely associated with high-quality blastocysts. A borderline statistically significant relationship was observed for male concentrations of mono(2-ethylhexyl) phthalate (OR = 0.52, 95% CI 0.27-1.00, P = 0.05) and cyclohexane-1,2-dicarboxylic acid-monocarboxy isooctyl ester (OR = 0.21, 95% CI 0.04-1.03, P = 0.05) at the blastocyst stage. Similar inverse associations were observed between male urinary phthalate metabolite concentrations and likelihood of transferrable quality blastocysts. For female partners, select metabolites were positively associated with odds of high or transferrable blastocyst quality, but the observed

associations were not consistent across blastocyst quality measures or between sex-specific and couples-level models. All models were adjusted for age of both partners, urinary metabolite concentrations of female partners and male infertility status, while models of blastocysts were additionally adjusted for embryo quality at cleavage stage.

LIMITATIONS, REASONS FOR CAUTION: Our modest sample included only 50 couples contributing one cycle each. In addition, non-differential misclassification of exposure remains a concern given the single-spot urine collection and the short half-life of phthalates.

WIDER IMPLICATIONS OF THE FINDINGS: Our results suggest an inverse association between male preconception concentrations of select phthalate metabolites and blastocyst quality, likely occurring after genomic activation. If corroborated with other studies, such findings will have public health and clinical significance for both the general population and those undergoing IVF.

STUDY FUNDING/COMPETING INTERESTS: This work was generously supported by grant K22-ES023085 from the National Institute of Environmental Health Sciences. The authors declare no competing interests.

TRIAL REGISTRATION NUMBER: N/A.

hero.3466600

Wu, W; Zhou, F; Wang, Y; Ning, Y; Yang, JY; Zhou, YK. (2017). Exposure to phthalates in children aged 5-7years: Associations with thyroid function and insulin-like growth factors. Sci Total Environ 579: 950-956. http://dx.doi.org/10.1016/j.scitotenv.2016.06.146.

This study aimed to evaluate the associations between phthalate concentrations and thyroid function in preschool children. We collected demographic data and biological samples from 216 children aged 5-7years. We calculated urinary concentrations of eight mono-phthalate metabolites (mPAEs) separately for children from urban and rural areas and investigated their associations with thyroid function and growth hormones. mPAE concentrations were higher in children from the urban area than in those from the rural area, and most mPAEs were positively associated with free triiodothyronine and free thyroxine. The insulin-like growth factor 1 (IGF-1) concentration decreased 0.082ng/mL (95% confidence interval [CI]: -1.34, -0.113) with each 1ng/mL increase in monomethyl phthalate (MMP) and 0.132ng/mL (95% CI: -0.209, -0.055) with each 1ng/mL increase in mono-n-butyl phthalate. The insulin-like growth factor binding protein 3 concentration decreased by 0.01mg/L (95% CI: -0.001, -0.000) or 0.01mg/L (95% CI: -0.003, -0.000) with each 1ng/mL increase in MMP or monoethyl phthalate, respectively. Exposure to some phthalates at 5-7years of age might interfere with thyroid hormones and growth.

hero.3469193

Wu, W; Zhou, F; Wang, Y; Ning, Y; Yang, JY; Zhou, YK. (2017). Phthalate levels and related factors in children aged 6-12 years. Environ Pollut 220: 990-996. http://dx.doi.org/10.1016/j.envpol.2016.11.049.

Although previous studies showed that children are widely exposed to phthalates, the sources of phthalate exposure for school-aged children in China are not well understood. This study aimed to assess phthalate metabolite levels and explore the factors influencing exposure in children. We collected demographic data and biological samples from 336 children aged 6-12 years. We calculated urinary concentrations of 14 mono-phthalate metabolites and conducted chi-square ($\chi(2)$) tests and logistic regression analysis to determine the variables associated with phthalate levels. Mono-n-butyl phthalate (MnBP) and mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) were the most abundant urinary phthalate metabolites. In addition, housing type, decorating materials in the home, and frequency of canned food consumption were associated with exposure to low molecular weight phthalates. Water source, duration of time spent playing with toys, residential area, and frequency of canned food consumption were associated with exposure to high molecular weight phthalates. Based on these results, potential strategies to reduce exposure to phthalates include avoiding plastic food containers and chemical fragrances as well as eating fewer processed foods, especially canned foods, and foods in plastic packaging.

hero.3469460

Wu, Y; Eichler, CM; Chen, S; Little, JC. (2016). Simple Method To Measure the Vapor Pressure of Phthalates and Their Alternatives. Environ Sci Technol 50: 10082-10088. http://dx.doi.org/10.1021/acs.est.6b02643.

Phthalates and alternative plasticizers are semivolatile organic compounds (SVOCs), an important class of indoor pollutants that may have significant adverse effects on human health. Unfortunately, models that predict emissions of and the resulting exposure to SVOCs have substantial uncertainties. One reason is that

the characteristics governing emissions, transport, and exposure are usually strongly dependent on vapor pressure. Furthermore, available data for phthalates exhibit significant variability, and vapor pressures for the various alternatives are usually unavailable. For these reasons, a new approach based on modeling of the evaporation process was developed to determine vapor pressures of phthalates and alternate plasticizers. A laminar flow forced convection model was used in the design of a partial saturator (PS) tube. The mass transfer mechanisms in the PS tube are accurately modeled and enable the determination of vapor pressure even when the carrier gas is not completely saturated, avoiding the complicated procedure to establish vapor saturation. The measured vapor pressures ranged from about 10(-2) to 10(-7) Pa. Compared to the traditional gas saturation method, the model-based approach is advantageous in terms of both predictability and simplicity. The knowledge provides new insight into experimental design and a sound basis for further method development.

hero.3357642

Xu, F; Giovanoulis, G; van Waes, S; Padilla-Sanchez, JA; Papadopoulou, E; Magnér, J; Haug, LS; Neels, H; Covaci, A. (2016). Comprehensive Study of Human External Exposure to Organophosphate Flame Retardants via Air, Dust, and Hand Wipes: The Importance of Sampling and Assessment Strategy. Environ Sci Technol 50: 7752-7760. http://dx.doi.org/10.1021/acs.est.6b00246.

We compared the human exposure to organophosphate flame retardants (PFRs) via inhalation, dust ingestion, and dermal absorption using different sampling and assessment strategies. Air (indoor stationary air and personal ambient air), dust (floor dust and surface dust), and hand wipes were sampled from 61 participants and their houses. We found that stationary air contains higher levels of ΣPFRs (median = 163 ng/m(3), IQR = 161 ng/m(3)) than personal air (median = 44 ng/m(3), IQR = 55 ng/m(3)), suggesting that the stationary air sample could generate a larger bias for inhalation exposure assessment. Tris(chloropropyl) phosphate isomers (ΣTCPP) accounted for over 80% of ΣPFRs in both stationary and personal air. PFRs were frequently detected in both surface dust (ΣPFRs median = 33100 ng/g, IQR = 62300 ng/g) and floor dust (ΣPFRs median = 20500 ng/g, IQR = 30300 ng/g). Tris(2-butoxylethyl) phosphate (TBOEP) accounted for 40% and 60% of ΣPFRs in surface and floor dust, respectively, followed by ΣTCPP (30% and 20%, respectively). TBOEP (median = 46 ng, IQR = 69 ng) and ΣTCPP (median = 37 ng, IQR = 49 ng) were also frequently detected in hand wipe samples. For the first time, a comprehensive assessment of human exposure to PFRs via inhalation, dust ingestion, and dermal absorption was conducted with individual personal data rather than reference factors of the general population. Inhalation seems to be the major exposure pathway for ΣTCPP and tris(2-chloroethyl) phosphate (TCEP), while participants had higher exposure to TBOEP and triphenyl phosphate (TPHP) via dust ingestion. Estimated exposure to ΣPFRs was the highest with stationary air inhalation (median =34 ngkg bw(-1)day(-1), IQR = 38 ngkg bw(-1)day(-1)), followed by surface dust ingestion (median = 13 ngkg bw(-1)day(-1), IQR = 28 ngkg bw(-1)day(-1)), floor dust ingestion and personal air inhalation. The median dermal exposure on hand wipes was 0.32 ngkg bw(-1)day(-1) (IQR = 0.58 ngkg bw(-1)day(-1)) for ΣTCPP. The selection of sampling and assessment strategies could significantly affect the results of exposure assessment.

hero.3469543 REVIEW

Yaghjyan, L; Ghita, GL; Dumont-Driscoll, M; Yost, RA; Chang, SH. (2016). Maternal exposure to di-2-ethylhexylphthalate and adverse delivery outcomes: A systematic review [Review]. Reprod Toxicol 65: 76-86. http://dx.doi.org/10.1016/j.reprotox.2016.07.002.

Adverse pregnancy outcomes, including preterm delivery, short gestational age, and abnormal birth weight, remain a public health concern. The evidence on the association of the most common phthalate, di-2-ethylhexyl phthalate (DEHP) with adverse pregnancy outcomes remains equivocal. This systematic review summarizes published studies that investigated the association of DEHP with preterm delivery, gestational age, and birthweight. A comprehensive literature search found 15 relevant studies, most of which evaluated more than one outcome (four studies for preterm delivery, nine studies for gestational age, and ten studies for birthweight). Studies varied greatly with respect to study design, exposure assessment, analytical methods, and direction of the associations. We identified important methodological concerns which could have resulted in selection bias and exposure misclassification and contributed to null findings and biased associations. Given limitations of the previous studies discussed in this review, more thorough investigation of these associations is warranted to advance our scientific knowledge.

hero.3350214

Yamazaki, H; Suemizu, H; Mitsui, M; Shimizu, M; Guengerich, FP. (2016). Combining Chimeric Mice with Humanized Liver, Mass Spectrometry, and Physiologically-Based Pharmacokinetic Modeling in Toxicology. Chem Res Toxicol. http://dx.doi.org/10.1021/acs.chemrestox.6b00136.

Species differences exist in terms of drug oxidation activities, which are mediated mainly by cytochrome P450 (P450) enzymes. To overcome the problem of species extrapolation, transchromosomic mice containing a human P450 3A cluster or chimeric mice transplanted with human hepatocytes have been introduced into the human toxicology research area. In this review, drug metabolism and disposition mediated by humanized livers in chimeric mice are summarized in terms of biliary/urinary excretions of phthalate and bisphenol A and plasma clearances of the human cocktail probe drugs caffeine, warfarin, omeprazole, metoprolol, and midazolam. Simulation of human plasma concentrations of the teratogen thalidomide and its human metabolites is possible with a simplified physiologically based pharmacokinetic model based on data obtained in chimeric mice, in accordance with reported clinical thalidomide concentrations. In addition, in vivo nonspecific hepatic protein binding parameters of metabolically activated (14)C-drug candidate and hepatotoxic medicines in humanized liver mice can be analyzed by accelerator mass spectrometry and are useful for predictions in humans.

hero.3350228

Yan, B; Guo, J; Liu, X; Li, J; Yang, X; Ma, P; Wu, Y. (2016). Oxidative stress mediates dibutyl phthalateinduced anxiety-like behavior in Kunming mice. Environ Toxicol Pharmacol 45: 45-51. http://dx.doi.org/10.1016/j.etap.2016.05.013.

Among all phthalate esters, dibutyl phthalate (DBP) is only second to di-(2-ethylhexyl) phthalate (DEHP) in terms of adverse health outcomes, and its potential cerebral neurotoxicity has raised concern in recent years. DBP exposure has been reported to be responsible for neurobehavioral effects and related neurological diseases. In this study, we found that neurobehavioral changes induced by DBP may be mediated by oxidative damage in the mouse brain, and that the co-administration of Mangiferin (MAG, 50mg/kg/day) may protect the brain against oxidative damage caused by DBP exposure. The results of ethological analysis (elevated plus maze test and open-field test), histopathological examination of the brain, and assessments of oxidative stress (OS) in the mouse brain showed that there is a link between oxidative stress and anxiety-like behavior produced by DBP at higher doses (25 or 125mg/kg/day). Biomarkers of oxidative stress encompass reactive oxygen species (ROS), glutathione (GSH), malondialdehyde (MDA) and DPC coefficients (DPC). MAG (50mg/kg/day),administered as an antioxidant,can attenuatetheanxiety-like behavior of the tested mice.

hero.3479535

Yan, J, in; Tang, B, in; Wu, D, i; Li, S; Xu, K; Ma, X; Wang, Q; Li, H, ui. (2016). Synthesis and characterization of beta-cyclodextrin/fraxinellone inclusion complex and its influence on interaction with human serum albumin. Spectros Lett 49: 542-550. http://dx.doi.org/10.1080/00387010.2016.1218898.

Aqueous solubility is one of the key determinants in developing new chemical entities as drugs. In this study, to improve the solubility of fraxinellone, a novel beta-cyclodextrin/ fraxinellone inclusion complex was prepared and characterized by Fourier transform infrared spectroscopy, thermogravimetric analysis, X-ray diffraction, and elemental analysis. Moreover, the influence of inclusion of small molecule by cyclodextrins on its binding with transporter in human body is essential for drug development. For the first time, we report the interaction of fraxinellone and its inclusion complex with human serum albumin. Fluorescence quenching of albumin by fraxinellone and its inclusion complex is a static process through complex formation. The results indicated that beta-cyclodextrin did not affect the binding force and site of fraxinellone to the protein. Furthermore, circular dichroism showed that both fraxinellone and its inclusion complex induced a significant change in the secondary structure of human serum albumin.

hero.3479531

Yang, R; Liu, Y; Yan, X; Liu, S. (2016). Simultaneous extraction and determination of phthalate esters in aqueous solution by yolk-shell magnetic mesoporous carbon-molecularly imprinted composites based on solid-phase extraction coupled with gas chromatography-mass spectrometry. Talanta 161: 114-121. http://dx.doi.org/10.1016/j.talanta.2016.08.037.

A rapid, sensitive and accurate method for the simultaneous extraction and determination of five types of trace phthalate esters (PAEs) in environmental water and beverage samples using magnetic molecularly imprinted solid-phase extraction (MMIP-SPE) coupled with gas chromatography-mass spectrometry (GC-MS) was developed. A novel type of molecularly imprinted polymers on the surface of yolk-shell magnetic mesoporous carbon (Fe3O4@void@C-MIPs) was used as an efficient adsorbent for selective adsorption of phthalate esters based on magnetic solid-phase extraction (MSPE). The real samples were first preconcentrated by Fe3O4@void@C-MIPs, subsequently extracted by eluent and finally determined by GC-MS after magnetic separation. Several variables affecting the extraction efficiency of the analytes, including the type and volume of the elution solvent, amount of adsorbent, extraction time, desorption time and pH of the sample solution, were investigated and optimized. Validation experiments indicated that the developed method presented good linearity (R(2)>0.9961), satisfactory precision (RSD<6.7%), and high recovery (86.1-103.1%). The limits of detection ranged from 1.6ng/L to 5.2ng/L and the enrichment factor was in the range of 822-1423. The results indicated that the novel method had the advantages of convenience, good sensitivity, and high efficiency, and it could also be successfully applied to the analysis of PAEs in real samples.

hero.3479514

Yue, Y; Sun, Y; Yan, X; Liu, J; Zhao, S; Zhang, J. (2016). Evaluation of the binding of perfluorinated compound to pepsin: Spectroscopic analysis and molecular docking. Chemosphere 161: 475-481. http://dx.doi.org/10.1016/j.chemosphere.2016.07.047.

In this paper, we investigated the binding mode of perfluorooctanoic acid (PFOA) and perfluorononanoic acid (PFNA) to pepsin using spectroscopies and molecular docking methods. Fluorescence quenching study indicated that their different ability to bind with pepsin. Meanwhile, time-resolved fluorescence measurements established that PFOA and PFNA quenched the fluorescence intensity of pepsin through the mechanism of static quenching. The thermodynamic parameters showed that hydrophobic forces were the main interactions. Furthermore, UV-vis, FTIR, three-dimensional fluorescence and molecular docking result indicated that PFCs impact the conformation of pepsin and PFOA was more toxic than PFNA. The conformational transformation of PFOA/PFNA-pepsin was confirmed through the quantitative analysis of the CD spectra. The present studies offer the theory evidence to analyze environmental safety and biosecurity of PFCs on proteases.

hero.3469370 REVIEW

Zarean, M; Keikha, M; Poursafa, P; Khalighinejad, P; Amin, M; Kelishadi, R. (2016). A systematic review on the adverse health effects of di-2-ethylhexyl phthalate. Environ Sci Pollut Res 23: 24642-24693. http://dx.doi.org/10.1007/s11356-016-7648-3.

Di (ethylhexyl) phthalate (DEHP) is a global environmental pollutant. This study aims to systematically review the literature on health effects of exposure to DEHP including effects on reproductive health, carcinogenesis, pregnancy outcome, and respiratory system. The literature search was done through Scopus, ISI Web of Science, Google Scholar, PubMed, Medline, and the reference lists of previous review articles to identify relevant articles published to June 2016 in each subject area. The inclusion criteria were as follows: original research, cross-sectional studies, case-control studies, cohort studies, interventional studies, and review articles. Both human and animal studies were included. The search was limited to English language papers. Conference papers, editorials, and letters were not included. The systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Overall, 152 of the 407 papers met the inclusion criteria. We provided an up-to-date comprehensive and critical assessment of both human and animal studies undertaken to explore the effects of DEHP. It revealed that in experimental studies, exposure to DEHP mainly targeted the reproductive, neurodevelopment, and respiratory systems. Human studies reported that exposure to this contaminant had carcinogenic effects and influenced neurodevelopment in early life. This systematic review underscored the adverse health effects of DEHP for pregnant women and the pediatric age group. It summarizes different response of humans and experimental animals to DEHP exposure, and some suggested underlying mechanisms.

hero.3469621

Zeliger, HI; Lipinski, B. (2015). Physiochemical basis of human degenerative disease. Interdiscip Toxicol 8: 15-21. http://dx.doi.org/10.1515/intox-2015-0003.

The onset of human degenerative diseases in humans, including type 2 diabetes, cardiovascular disease, neurological disorders, neurodevelopmental disease and neurodegenerative disease has been shown to be related to exposures to persistent organic pollutants, including polychlorinated biphenyls, chlorinated pesticides, polybrominated diphenyl ethers and others, as well as to polynuclear aromatic hydrocarbons, phthalates, bisphenol-A and other aromatic lipophilic species. The onset of these diseases has also been related to exposures to transition metal ions. A physiochemical mechanism for the onset of degenerative environmental disease dependent upon exposure to a combination of lipophilic aromatic hydrocarbons and transition metal ions is proposed here. The findings reported here also, for the first time, explain why aromatic hydrocarbons exhibit greater toxicity than aliphatic hydrocarbons of equal carbon numbers.

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Zhang, G; Ling, X; Liu, K; Wang, Z; Zou, P; Gao, J; Cao, J; Ao, L. (2016). The p-eIF2α/ATF4 pathway links endoplasmic reticulum stress to autophagy following the production of reactive oxygen species in mouse spermatocyte-derived cells exposed to dibutyl phthalate. Free Radic Res 50: 698-707. http://dx.doi.org/10.3109/10715762.2016.1169403.

Dibutyl phthalate (DBP) is a widely used plasticizer that has been shown to induce germ cell apoptosis-related testicular atrophy and cause reproductive toxicity. Our previous results indicated that endoplasmic reticulum (ER) stress-activated autophagy served as a self-defense mechanism against DBP-induced germ cell apoptosis. However, the specific pathways that link ER stress and autophagy remain unclear. Here, we showed that exposure to DBP enhanced autophagic flux in mouse spermatocyte-derived GC-2 cells and that the eukaryotic translation initiation factor 2/activating transcription factor 4 pathway mediated ER stress-related autophagy independent of the mTOR and Beclin-1 pathways. Moreover, we demonstrated that DBP treatment led to the generation of reactive oxygen species (ROS) and that the inhibition of ROS by melatonin abrogated both ER stress and autophagy. The results indicated that excessive ROS production might be involved in DBP-induced ER stress and autophagy in GC-2 cells. Thus, ROS may serve as upstream mediators of ER stress and autophagy in DBP-treated GC-2 cells.

hero.3420616

Zhang, H; Xie, J; Yoshino, H; Yanagi, U; Hasegawa, K; Kagi, N; Lian, Z. (2016). Thermal and environmental conditions in Shanghai households: Risk factors for childhood health. Build Environ 104: 35-46. http://dx.doi.org/10.1016/j.buildenv.2016.04.020.

An overall investigation of children's health status, residential thermal environment, and pollutants was conducted in the homes primary school children during winter and summer in Shanghai, China. The houses were divided into Group A (unhealthy child living) and Group B (healthy child living). During a two-week monitoring period in winter, indoor temperatures in Group A were significantly lower than in Group B (1-2 degrees C; $p < 0.001$). Relative humidity (RH) of Group A were 5-8% higher than Group B ($p < 0.001$), and the ratio of RH > 70% of Group A was around 0.6 in winter. Bad thermal environment in Group A was a risk factor for children's health. Average winter CO2 concentrations were 758 ppm in Group A and 701 ppm in Group B, and the houses had poor ventilation during nighttime. Indoor concentrations of formaldehyde (HCHO), acetaldehyde and TVOC generally satisfied the Chinese national standards. However, indoor PM2.5 and PM10 concentrations in Group A were higher than those of Group B, and PM concentrations in all investigated houses exceeded the Chinese national standards in winter. Dibutyl phthalate (DBP) and Di (2-ethylhexyl) phthalate (DEHP) in house dust of four living rooms showed very high concentrations (3-4 times the EU recommended limit of 1000 mu g/g). Aspergillus and Cladosporium in room air and house dust were linked to high RH, and could be suspected association with poor children's health. This study provides comprehensive information on indoor thermal and environmental conditions in houses in Shanghai, and their exposures of primary schoolchildren to these health risks. (C) 2016 Elsevier Ltd. All rights reserved.

hero.3479534

Zhang, J; Jin, S; Zhao, J; Li, H. (2016). Effect of dibutyl phthalate on expression of connexin 43 and testosterone production of leydig cells in adult rats. Environ Toxicol Pharmacol 47: 131-135. http://dx.doi.org/10.1016/j.etap.2016.09.010.

To investigate the adverse effect of dibutyl phthalate (DBP) on Leydig cells and its mechanism related to gap junction, Leydig cells isolated from adult rats were treated with 0.1% dimethylsulfoxide (DMSO), 50mg/L DBP, 50mg/L DBP+10μM prostaglandin E2 (PGE2) and 40μM flutamide respectively. Radioimmunoassay, semi-quantitative RT-PCR, immunofluorescence and Western blot were applied to determine the expression of testosterone and Connexin 43 (Cx43) in Leydig cells. The expression of testosterone and Cx43 were both decreased in DBP group (P<0.05). While Cx43 was up-regulated after administered to PGE2, there was no significant change in testosterone. However, testosterone was down-regulated with a significant decrease of Cx43 in flutamide group. The results indicated that the inhibitory effect of DBP on testosterone production was not through the down-regulation of Cx43. On the contrary, the change of testosterone can influence the expression of Cx43 in Leydig cells.

hero.3350205

Zhang, L; Jiang, DG; Sui, HX; Wu, PG; Liu, AD; Yang, d; Liu, ZP; Song, Y; Li, N. (2016). Dietary Exposure to Benzyl Butyl Phthalate in China. Biomed Environ Sci 29: 365-373. http://dx.doi.org/10.3967/bes2016.047. OBJECTIVE: Benzyl butyl phthalate (BBP) is a plasticizer used in food contact materials. Dietary exposure to BBP might lead to reproduction and developmental damages to human. The present paper was aimed to assess the health risk of BBP dietary exposure in Chinese population.

METHODS: The BBP contents were detected in 7409 food samples from 25 food categories by gas chromatography-mass spectrometry operated in selected ion monitoring (SIM) mode. The dietary exposures of BBP in different age and sex groups were estimated by combining the content data with food consumption data derived from 2002 China National Nutrient and Health Survey, and evaluated according to the tolerable daily intake (TDI) of BBP established by European Food safety Agency.

RESULTS: It was found that BBP was undetectable in most samples and the highest level was 1.69 mg/kg detected in a vegetable oil sample. The average dietary exposure of BBP in people aged 2 years was 1.03 μg/kg bw per day and the highest average exposure was found in 2-6 years old children (1.98 μg/kg bw per day). The BBP exposure in 7-12 months old children excessed 10% of tolerable daily intake (TDI) in worst scenario. .

CONCLUSION: The health risk of BBP dietary exposure in Chinese population is low and, considering BBP alone, there is no safety concern.

hero.3469476

Zhang, T; Shen, W; De Felici, M; Zhang, XF. (2016). Di(2-ethylhexyl)phthalate: Adverse effects on folliculogenesis that cannot be neglected [Review]. Environ Mol Mutagen 57: 579-588. http://dx.doi.org/10.1002/em.22037. Primordial follicle formation and the subsequent transition of follicles through primary and secondary stages constitute crucial events of oogenesis. In particular, in mammals, defects in the processes that precede and accompany the formation of the primordial follicle pool can affect the size of this population significantly, while alterations in follicle activation, growth and maturation can result in premature depletion of the follicle reserve or cause follicle arrest at immature stages. Over the last decade, in vitro and in vivo approaches have been used to provide evidence that exposure to di(2-ethylhexyl)phthalate(DEHP), the most widely used plasticizer, has a deleterious effect on various stages of folliculogenesis in rodents. There is growing concern, supported by epidemiological and experimental data, that DEHP may have similar effects in women. This article reviews the evidence, with particular reference to our own findings, that DEHP may actually exert a variety of adverse effects on mammalian folliculogenesis from early to final stages of oogenesis, including altered development of the primordial germ cells, impaired fetal oocyte survival and meiotic progression, reduced oocyte nest breakdown, acceleration of primordial follicle activation, altered follicle steroidogenesis and increased follicle atresia. These effects can cause serious complications for reproductive and nonreproductive women's health. In addition, emerging data indicate that phthalates, including DEHP, may cause subtle epigenetic changes in germ cells that can be transmitted to subsequent generations, with potential negative effects on human health. Environ. Mol. Mutagen. 57:589-604, 2016. 2016 Wiley Periodicals, Inc.

hero.3466570

Zhang, W; Shen, XY; Zhang, WW; Chen, H; Xu, WP; Wei, W. (2016). Di-(2-ethylhexyl) phthalate could disrupt the insulin signaling pathway in liver of SD rats and L02 cells via PPARγ. Toxicol Appl Pharmacol 316: 17-26. http://dx.doi.org/10.1016/j.taap.2016.12.010.

Di-(2-ethylhexyl)-phthalate (DEHP), a ubiquitous industrial pollutant in our daily life, has been reported to cause adverse effects on glucose homeostasis and insulin sensitivity in epidemiological studies previously. Recently, it has been reported to be an endocrine disrupter and ligand to peroxisome proliferator activated receptor, which could influence the homeostasis of liver metabolic systems and contribute to the development of type-2 diabetes. However, the potential mechanisms are not known yet. This study was designed to solve these problems with male SD rats and normal human hepatocyte line, L02 cells, exposed to DEHP for toxicological experiments. Adult male SD rats were divided into four groups, normal group fed with regular diets and three DEHP-treated groups (dissolved in olive oil at doses of 0.05, 5 and 500mg/kg body weight, respectively, once daily through gastric intubations for 15weeks). L02 cells were divided into 6 groups, normal group with 5, 10, 25, 50, and 100μmol/l DEHP groups. DEHP-exposed rats exhibited significant liver damage, glucose tolerance, and insulin tolerance along with reduced expression of insulin receptor and GLUT4 proteins in the liver tissues. The results of in vitro experiments could determine that the DEHP-induced activation of peroxisome proliferator activated receptor γ (PPARγ) played a key role in the production of oxidative stress and down-regulated expression of insulin receptor and GLUT4 proteins in L02 cells. This conclusion could be supported by the results of in vitro experiments, in which the cells were exposed to DEHP with GW9662 (PPARγ inhibitor). In general, these results highlight the key role of PPARγ in the process of insulin resistance induced by DEHP.

hero.2967076

Zhao, JF; Hsiao, SH; Hsu, MH; Pao, KC; Kou, YR; Shyue, SK; Lee, TS. (2014). Di-(2-ethylhexyl) phthalate accelerates atherosclerosis in apolipoprotein E-deficient mice. Arch Toxicol 90: 181-190. http://dx.doi.org/10.1007/s00204-014-1377-5.

Di-(2-ethylhexyl) phthalate (DEHP) is associated with atherosclerosis-related cardiovascular disease complications, but we lack direct evidence of its unfavorable effect on atherogenesis. In this study, we aimed to clarify in vivo and in vitro the contribution of DEHP to the development of atherosclerosis and its underlying mechanisms. Apolipoprotein E-deficient (apoE(-/-)) mice chronically treated with DEHP for 4weeks showed exacerbated hyperlipidemia, systemic inflammation, and atherosclerosis. In addition, DEHP promoted low-density lipoprotein (LDL) oxidation, which led to inflammation in endothelial cells as evidenced by increased protein expression of pro-inflammatory mediators. Furthermore, chronic DEHP treatment increased hepatic cholesterol accumulation by downregulating the protein expression of key regulators in cholesterol clearance including LDL receptor, cholesterol 7α-hydrolase, ATP-binding cassette transporter G5 and G8, and liver X receptor α. Moreover, the adiposity and inflammation of white adipose tissues were promoted in DEHP-treated apoE(-/-) mice. In conclusion, DEHP may disturb cholesterol homeostasis and deregulate the inflammatory response, thus leading to accelerated atherosclerosis.

hero.3469398

Zhao, Y; Chen, J; Wang, X; Song, Q; Xu, HH; Zhang, YH. (2016). Third trimester phthalate exposure is associated with DNA methylation of growth-related genes in human placenta. Sci Rep 6: 33449. http://dx.doi.org/10.1038/srep33449.

Strong evidence implicates maternal phthalate exposure during pregnancy in contributing to adverse birth outcomes. Recent research suggests these effects might be mediated through the improper regulation of DNA methylation in offspring tissue. In this study, we examined associations between prenatal phthalate exposure and DNA methylation in human placenta. We recruited 181 mother-newborn pairs (80 fetal growth restriction newborns, 101 normal newborns) in Wenzhou, China and measured third trimester urinary phthalate metabolite concentrations and placental DNA methylation levels of IGF2 and AHRR. We found urinary concentrations of mono (2-ethyl-5- hydroxyhexyl) phthalate (MEHHP), and mono (2-ethyl-5-oxohexyl) phthalate (MEOHP) were significantly inversely associated with placental IGF2 DNA methylation. The associations were much more evident in fetal growth restriction (FGR) newborns than those in normal newborns. These findings suggest that changes in placental DNA methylation might be part of the underlying biological pathway between prenatal phthalate exposure and adverse fetal growth.

hero.3466573

Zhou, C; Flaws, JA. (2016). Effects of an environmentally relevant phthalate mixture on cultured mouse antral follicles. Toxicol Sci. http://dx.doi.org/10.1093/toxsci/kfw245.

Phthalates are used in building materials, medical devices, and personal care products. Most studies on phthalates have focused on single phthalates, but it is important to study mixtures of phthalates because humans are exposed to such mixtures daily. We tested the hypothesis that phthalate mixture exposure decreases antral follicle growth, compromises steroidogenic capacity, and induces atresia. Antral follicles from adult CD-1 mice were cultured with vehicle control or phthalate mixture (1-500 µg/ml) for 96 hours. The mixture was made of 35% diethyl phthalate, 21% di(2-ethylhexyl) phthalate, 15% dibutyl phthalate, 15% diisononyl phthalate, 8% diisobutyl phthalate, and 5% benzylbutyl phthalate. During culture, antral follicle diameters were measured every 24 hours to monitor growth. After culture, media were subjected to measurements of sex steroid hormones and follicles were subjected to evaluation of gene expression and atresia. The phthalate mixture (100 and 500 µg/ml) decreased antral follicle growth starting at 24 hours compared to controls. The mixture at 10, 100, and 500 µg/ml also decreased androstenedione, testosterone, estrone, and estradiol levels compared to control. The mixture (10, 100, and 500 µg/ml) reduced atresia rating, but it induced more oocyte fragmentation compared to control. The phthalate mixture at different doses adversely affected cell cycle regulators, antioxidant enzymes, apoptotic factors, steroidogenic enzymes, and receptors. Collectively, these data indicate that exposure to an environmentally relevant phthalate mixture reduces antral follicle growth, induces oocyte fragmentation, and decreases hormone production by adversely affecting the expression of cell cycle regulators, apoptotic factors, steroidogenic enzymes, and receptors.

hero.3070917

Zhou, J; Cao, X; Lin, H; Ni, Z; He, Y; Chen, M; Zheng, H; Chen, X. (2015). Safety and effectiveness evaluation of a domestic peritoneal dialysis fluid packed in non-PVC bags: study protocol for a randomized controlled trial. Trials 16: 592. http://dx.doi.org/10.1186/s13063-015-1131-1.

BACKGROUND: Peritoneal dialysis is an important type of renal replacement therapy for uremic patients. In peritoneal dialysis, fluids fill in and flow out of the abdominal cavity three to five times per day. Usually, the fluid is packed in a polyvinyl chloride (PVC) bag. Safety concerns have arisen over di-(2-ethylhexyl) phthalate, which is essential in the formation of PVC materials. In 2011, the National Development and Reform Commission of China released a catalog of industrial structural adjustments, mandating the elimination of PVC bags for intravenous infusion and food containers. Although bags for peritoneal dialysis fluid were not included in the elimination list, several manufacturers began to develop new materials for fluid bags. HUAREN peritoneal dialysis fluid consists of the same electrolytes and buffer agent as in Baxter fluid, but is packed in bags that do not contain PVC. This multicenter randomized controlled trial was designed to compare peritoneal dialysis fluid packed in non-PVC-containing and PVC-containing bags. Further, the study sought to determine the proper dose of peritoneal dialysis fluid and the actual survival rates of Chinese patients undergoing peritoneal dialysis.

METHODS/DESIGN: The study participants are adults undergoing continuous ambulatory peritoneal dialysis for 30days to 6months. All eligible patients are randomized (1:1) to peritoneal dialysis with Baxter and HUAREN dialysis fluids (initial dose, 6l/day), with dosages adjusted according to a unified protocol. The primary outcomes are the 1-, 2-, 3-, 4-, and 5-year overall survival rates. Secondary outcome measures include technique survival rates, reductions in estimated glomerular filtration rate, nutritional status, quality of life, cardiovascular events, medical costs and drop-out rates. Safety outcome measures include adverse events, changes in vital signs and laboratory parameters, peritonitis, allergies, and quality of products.

DISCUSSION: This study is the first to evaluate the long-term safety and effectiveness of a non-PVC packed peritoneal dialysis fluid. The effects of plasticizer on patient long-term survival will be determined. The characteristics of Chinese patients undergoing peritoneal dialysis will be determined, including proper dose, technique survival rates, patient survival rates, and medical costs.

TRIAL REGISTRATION: Clinicaltrials.gov NCT01779557 .

hero.3070899

Zhu, Y; Hua, R; Zhou, Y; Li, H; Quan, S; Yu, Y. (2016). Chronic exposure to mono-(2-ethylhexyl)-phthalate causes endocrine disruption and reproductive dysfunction in zebrafish. Environ Toxicol Chem 35: 2117-2124. http://dx.doi.org/10.1002/etc.3369.

Phthalic acid esters are frequently detected in aquatic environment. In this study, zebrafish were exposed to low concentrations (0, 0.46, 4.0, and 37.5 µg/L) of mono-(2-ethylhexyl) phthalate (MEHP) for 81 days, and the

effects on reproduction, gamete quality, plasma vitellogenin (VTG), sex steroids, and transcriptional profiles of key genes involved in steroidogenesis were investigated. The results demonstrated that egg production and sperm quality were decreased upon exposure to MEHP, which also resulted in reduced egg diameter and eggshell as well as decreased egg protein content. Significant inductions in plasma testosterone and 17β-estradiol were observed in females, which might be resulted from the up-regulation of CYP19a and 17β-HSD gene transcription in the ovary. A significant increase in plasma E2 along with a decrease in plasma 11-keto testosterone was also observed in males, which was accompanied by the up-regulation of CYP19a and inhibition of CYP11b transcription in the testis. In addition, plasma vitellogenin levels were significantly increased after MEHP exposure in both sexes. Moreover, continuous MEHP exposure in the F1 embryos resulted in worse hatching rates and increased malformation rates compared to those without MEHP exposure. Taken together, these results demonstrate that MEHP has the potential to cause reproductive dysfunction and impair the development of offspring. However, it should be noted that most significant effects were observed at higher concentrations, and MEHP at typically measured concentrations may not have major effects on fish reproduction and development. This article is protected by copyright. All rights reserved.

hero.3469257

Zidek, A; Macey, K; Mackinnon, L; Patel, M; Poddalgoda, D; Zhang, Y. (2016). A review of human biomonitoring data used in regulatory risk assessment under Canada's Chemicals Management Program [Review]. Int J Hyg Environ Health. http://dx.doi.org/10.1016/j.ijheh.2016.10.007.

As a part of the Chemicals Management Plan launched in 2006, the Government of Canada is assessing and managing, where appropriate, the potential health and ecological risks associated with approximately 4300 substances under the Canadian Environmental Protection Act (1999). Since that time, nearly 3000 substances have been assessed, with human biomonitoring (HBM) data playing an increasingly important role for some substances. Case studies are presented, including both inorganic and organic substances (i.e., selenium, triclosan, phthalates), which highlight the impact and overall role HBM has had in regulatory decision making in Canada for these three substances as well as criteria used in the application of HBM data in human health risk assessment. An overview of its limitations in terms of how and when HBM data can be applied, when assessing human health in a regulatory setting, is discussed as well as the role HBM data can play in priority setting.

hero.3469547 REVIEW

Zlatnik, MG. (2016). Endocrine-Disrupting Chemicals and Reproductive Health [Review]. J Midwifery Womens Health 61: 442-455. http://dx.doi.org/10.1111/jmwh.12500.

This review discusses the evidence linking industrial chemicals to a variety of health and reproductive outcomes. Industrial chemical production has increased over the past 30 to 40 years. Basic science, animal models, and epidemiologic data suggest that certain chemicals may act as endocrine disruptors (substances that interfere with normal hormonal action) and may play an etiologic role in a number of conditions whose incidence has also increased during this same period. These include low birth weight, gestational diabetes, obesity, certain cancers, certain birth defects, and neurodevelopmental disorders such as attention deficit disorder and autism. In addition, some environmental chemicals may have epigenetic effects, resulting in transgenerational health impacts. The epidemiologic and experimental evidence that links chemicals such as plasticizers (eg, phthalates and phenols), flame retardants, perfluorinated compounds, and pesticides with adverse reproductive health outcomes is reviewed. Women's health care providers are the liaison between scientific research and their patients; they should educate themselves on the significance of environmental toxins to health. They are ideally positioned, not only to counsel and reassure pregnant women, but also to suggest practicable changes in dietary and lifestyle habits to improve their health. Furthermore, women's health care providers should advocate for regulatory changes that protect women and their families from the health effects of environmental toxins.