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INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

CRI's ICEIT has been designated as a
"UNEP Centre of Excellence for Environmental and Industrial Toxicology".

The Minderoo-Monaco Commission on Plastics and Human Health

The Minderoo-Monaco Commission on Plastics and Human Health aimed to comprehensively examine plastics' impacts on (1) human health and well-being; (2) the global environment; (3) the economy; and (4) vulnerable populations, towards offering science-based recommendations designed to support development of a Global Plastics Treaty, protect human health, and save lives.

Plastics are complex, highly heterogeneous, synthetic chemical materials. They are comprised of a carbon-based polymer backbone and thousands of additional chemicals that are incorporated into polymers to convey specific properties such as flexibility, stability, and flame retardation, many of these added chemicals being highly toxic.

Annual global plastic production volume has grown from under 2 megatons (Mt) in 1950 to 460 Mt in 2019, a 230-fold increase, and is on track to triple by 2060. Single-use plastics account for 35-40% of current plastic production and represent the most rapidly growing segment of plastic manufacture.

Plastics manufacture is energy-intensive and contributes significantly to climate change. At present, plastic production is responsible for an estimated 3.7% of global greenhouse gas emissions, and this is projected to increase to 4.5% by 2060 if current trends continue unchecked.

The plastic life cycle has three phases: production, use, and disposal.

In production, carbon feedstocks are transformed through energy-intensive, catalytic processes into a vast array of products. Plastic use occurs in every aspect of modern life and results in widespread human exposure to the chemicals contained in plastic.

Plastics disposal is highly inefficient, with recovery and recycling rates below 10% globally. Strategies for disposal of plastic waste include controlled and uncontrolled landfilling, open burning, thermal conversion, and export. Vast quantities of plastic waste are exported each year from high-income to low-income countries, where it accumulates in landfills, pollutes air and water, degrades vital ecosystems, befouls beaches and estuaries, and harms human health and environmental injustice on a global scale.

Environmental impacts: Plastics and plastic-associated chemicals contaminate aquatic, terrestrial, and atmospheric environments. The ocean is the ultimate destination, and plastics are found in coastal regions, the sea surface, the deep sea, and polar sea ice. Many plastics could persist in the global environment for decades. Macro- and micro-plastic particles have been identified in hundreds of marine species, including those consumed by humans. Trophic transfer of microplastic particles has been demonstrated.

Although microplastic particles themselves (>10 µm) appear not to undergo biomagnification, hydrophobic plastic-associated chemicals bioaccumulate in marine animals and bio-magnify in marine food webs. The amounts and fates of smaller microplastic and nanoplastic particles (MNPs <10 µm) in aquatic environments are poorly understood, but the potential for harm is worrying given their mobility in biological systems. MNP contamination of seafood results in direct human exposure to plastics and plastic-associated chemicals.

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The Minderoo-Monaco Commission on Plastics and Human Health

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Health impacts: Coal miners, oil workers and gas field workers who extract fossil carbon feedstocks for plastic production suffer increased mortality from traumatic injury, coal workers' pneumoconiosis, silicosis, cardiovascular disease, chronic obstructive pulmonary disease, and lung cancer.

Plastic production workers are at increased risk of leukemia, lymphoma, hepatic angiosarcoma, brain cancer, breast cancer, mesothelioma, neurotoxic injury, and decreased fertility.

Workers producing plastic textiles die of bladder cancer, lung cancer, mesothelioma, and interstitial lung disease at increased rates.

Plastic recycling workers have increased rates of cardiovascular disease, toxic metal poisoning, neuropathy, and lung cancer.

Residents of "Fenceline" communities adjacent to plastic production and waste disposal sites experience increased risks of premature birth, low birth weight, asthma, childhood leukemia, cardiovascular disease, chronic obstructive pulmonary disease, and lung cancer. During use and disposal, plastics release toxic chemicals, including additives and residual monomers, into the environment and into people. National biomonitoring surveys in the USA document population-wide exposures to these chemicals.

Plastic additives disrupt endocrine function and increase risk for premature births, neurodevelopmental disorders, male reproductive birth defects, infertility, obesity, cardiovascular disease, renal disease, and cancers.

Chemical-laden MNPs formed through the environmental degradation of plastic waste can enter living organisms, including humans. Emerging evidence indicates that MNPs may cause toxicity due to their physical and toxicological effects as well as by acting as vectors that transport toxic chemicals and bacterial pathogens into tissues and cells.

Infants in the womb and young children are at particularly high risk of plastic-related health effects. Plastic-associated exposures are linked to increased risks of prematurity, stillbirth, low birth weight, birth defects of the reproductive organs, neurodevelopmental impairment, impaired lung growth, and childhood cancer. Early-life exposures also increase the risk of multiple non-communicable diseases later in life.

Economic Impacts: In 2015, the health-related costs of plastic production were estimated to exceed $250 billion globally, and in the USA alone the health costs of disease and disability caused by the plastic-associated chemicals was estimated to exceed $920 billion.

Using the US Environmental Protection Agency's (EPA) social cost of carbon metric, the annual costs of plastics production-associated greenhouse gas emissions were estimated to be $341 billion. These almost certainly underestimate the full economic losses resulting from plastics' negative impacts on human health and the global environment.

Social impacts: The adverse effects of plastics and plastic pollution are not evenly distributed. They disproportionately affect poor, disempowered, and marginalized populations that had little to do with creating the current plastics crisis and lack the political influence or the resources to address it.

Social and environmental justice (SEJ) principles require reversal of these inequitable burdens to ensure that no group bears a disproportionate share of plastics' negative impacts and that those who benefit economically from plastics bear their fair share of its currently externalized costs.

Conclusions: Current patterns of plastic production, use, and disposal are not sustainable and are responsible for significant harms to human health, the environment, and the economy, as well as for deep societal injustices.

The main driver is an almost exponential and still accelerating increase in global plastic production. Plastics' harms are further magnified by low rates of recovery and recycling and by the long persistence of plastic waste in the environment. Chemicals in plastics are responsible for many of plastics' known harms to human and planetary health. The chemicals leach out of plastics, enter the environment, and result in human exposure and disease. All efforts to reduce plastics' hazards must address the hazards of plastic-associated chemicals.

Recommendations: The Commission supports urgent adoption of a strong and comprehensive Global Plastics Treaty in accord with the mandate set forth in the March 2022 resolution of the United Nations Environment Assembly (UNEA). It urges that a cap on global plastic production with targets, timetables, and national contributions be a central provision of the Global Plastics Treaty:

The Commission also encourages inclusion of a provision calling for exploration of listing some plastic polymers as persistent organic pollutants (POPs) under the Stockholm Convention. It also encourages a strong interface between the Global Plastics Treaty and the Basel and London Conventions to enhance management of hazardous plastic waste and slow current massive exports of plastic waste into the world's least-developed countries.

The Commission also recommends the creation of a Permanent Science Policy Advisory Body to guide the Treaty's implementation. The main priorities of this Body would be to guide Member States and other stakeholders in evaluating which solutions are most effective in reducing plastic consumption, enhancing plastic waste recovery and recycling, and curbing the generation of plastic waste. It could also assess trade-offs among these solutions and evaluate safer alternatives to current plastics, monitor the transnational export of plastic waste, and coordinate robust oceanic, land, and air-based MNP monitoring programs.

Finally, the Commission recommends urgent investment by national governments in research into solutions to the global plastic crisis, including determining which solutions are most effective and cost-effective. Oceanographic and environmental research is also needed to better measure concentrations and impacts of plastics <10 μm and understand their distribution and fate in the environment. Biomedical research is needed to elucidate the human health impacts of plastics.

Source: Annals of Global Health, Vol. 89, Issue 1, Article 23, March 2023.

Face Mask: Human Exposure to Microplastics and Phthalates

Wearing masks has become the norm during the Coronavirus disease pandemic, with 129 billion masks used every month in 2020. Although surgical masks, N95 respirators, and similar masks yield a more significant protective effect than other masks, they are often costly. As a result, activated carbon masks, cotton masks, and fashion masks have gained significant momentum.

Disposable masks are made of polymers such as polypropylene, polyurethane, polyacrylonitrile, polystyrene, polycarbonate, polyethylene, or polyester. In addition, phthalate esters, a common kind of plastic additives, have been detected in facemasks with a level up to 38 μg/g.

Once inhaled, part of microplastics keep away from the clearing mechanism of the respiratory tract and may lead to lung disease, such as asthma, chronic obstructive pulmonary disease, and even cancer, by producing radical oxygen species, inducing inflammation, damaging cellular structures, and blocking vessels.

Phthalate esters, typical endocrine disrupters, can enter the body through dermal contact and inhalation while wearing masks and result in a series of endocrine disorders.

A recent study found that masks released fibrous microplastics after 720h but did not consider the indoor and outdoor conditions, and the interval time was excessively long, as the average wearing time of masks was less than 24h.

Although the estimated daily intake of phthalate esters based on the content reduction after degassing the mask has been calculated, about 2.0-20 ng/kg bw/day for adults, release characteristics of phthalate esters and various masks' different effects on exposure were not concerned. Moreover, it is widely thought that masks represent a protector of human exposure to microplastics and phthalates. Overwhelming evidence substantiates that these pollutants are widely distributed in the air, with a definite risk of inhalation exposure when people do not wear masks. Therefore, whether facemasks increase or decrease exposure to microplastics and phthalates remains uncertain.

In the present study, an experimental device was set up to simulate the impact of five kinds of masks (activated-carbon, N95, surgical, cotton, and fashion masks) on the risk of humans inhaling microplastics and phthalates during wearing.

The residual concentrations of seven major phthalates ranged from 296 to 72,049 ng/g, with the lowest and the highest concentrations detected in surgical and fashion masks, respectively. These results indicate that facemasks also represent an important source of phthalate esters exposure in daily life and warrant further study.

During the whole inhalation simulation process, fragmented and 20-100 μm microplastics accounted for the largest, with a rapid release during the first six hours. After one day's wearing, that of 6 h, while wearing different masks, 25-135 and 65-298 microplastics were inhaled indoors and outdoors, respectively.

The total estimated daily intake of phthalates with indoor and outdoor conditions by inhalation and skin exposure ranged from 1.2 to 13 and 0.43 to 14 ng/kg bw/day, respectively.

In conclusion, surgical masks play a protective role, while wearing activated carbon, cotton, and fashion masks in indoor and outdoor environments increases human exposure to phthalate esters. Additionally, wearing cotton masks resulted in a larger inhalation risk than wearing no mask, while other types of masks acted as protectors against microplastics.

However, more studies and development are needed based on some limitations including limited number of masks, and laboratory conditions which might be an overestimation of the microplastic exposure.

The study corroborates that cotton and fashion masks are important sources of human exposure to microplastics and phthalates, highlighting that it is not recommended to wear these two masks unnecessarily in daily life to reduce exposure. In contrast, the surgical mask is a great choice against microplastics and phthalates, as well as the COVID-19 virus.

Source: Toxics, Vol. 11, No. 2, Article 87, January 2023.

Unexpected Air Pollutants with Potential Human Health Hazards

Global chemical pollution has increased dramatically in recent decades, leading to various potential risks that exceed society's ability to conduct safety-related assessments and monitoring.

When it comes to agriculture's contribution to air pollution, synthetic pesticides are often considered. Ambient air contamination with agrochemicals would be related to surrounding land use, as a result of application-related drift or via wind-blown soil particles. In contrast, chemicals of non-agricultural origins should be less related to agricultural land use and more influenced by meteorological parameters.

To better understand the influence of land use and meteorological parameters on air pollutants, the present study was conducted in 15 regions with different land use in eastern Austria to (i) assess the environmental exposure to chemicals other than agricultural pesticides via passive air sampling, (ii) examine the influence of surrounding land use and meteorological parameters on local contamination levels, and (iii) review the potential toxicological hazards of these exposures to humans and the environment based on globally harmonized hazard statements for the detected substances.

The findings of this study reported that, in addition to agricultural pesticides, eight other substances were frequently detected in ambient air: Nitrapyrin, a nitrification inhibitor used to increase

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Air Pollution Exposure and Osteoporosis Risk

Long-term ambient air pollution exposure is related to the increased risk of complex diseases such as cardiovascular diseases, respiratory diseases, malignant tumors, and increased morbidity and mortality worldwide.

Osteoporosis is a systemic bone disease characterized by low bone mineral density, bone fragility, and devastation of the microstructure of bone tissue, which occurs when bone destruction exceeds new bone formation.

Previous studies have shown inconsistent associations between air pollution exposure and the risk of osteoporosis and fracture. These inconsistent results may contribute to heterogeneity in the basic characteristics of subjects, study design, sample size, measurement of outcomes, and covariate correction during the analysis of various studies.

Previous studies have typically focused on the association of a single air pollutant with disease risk, while largely ignoring the combined effects of various air pollutants. More importantly, it is still unknown how air pollutants interact with genetic factors in determining the risk of osteoporosis.

Based on large-scale data from the UK Biobank, a systemic study was conducted to test associations between osteoporosis risk and exposure to environmental air pollutants in either single or multiple patterns, and also to test the joint effects of air pollution and genetic factors on the risk of osteoporosis.

The researchers used the Land Use Regression models, developed by the European Study of Cohorts for Air Pollution Effects (ESCAPE) project, to calculate the estimated annual average concentrations of ambient air pollution, including $PM_{2.5}$, $PM_{2.5-10}$, PM_{10}, nitrogen dioxide (NO_2), and nitrogen oxide (NOx).

Air pollution scores (APS) were constructed to assess the combined effects of multiple air pollutants on osteoporosis risk.

A genetic risk score (GRS) was also constructed based on a large genome-wide association study of femoral neck bone mineral density and assessed whether single or combined exposure to air pollutants modifies the effect of genetic risk on osteoporosis and fracture risk.

The results showed that $PM_{2.5}$, NO_2, NOx, and APS were significantly associated with an increased risk of osteoporosis and fracture.

In this large-scale prospective study, PM2.5 was significantly associated with the risk of osteoporosis and fracture, which is consistent with previous epidemiological studies. In this analysis, researchers detected a significant effect of increased PM_{10} concentration on estimated bone mineral density but no significant association with osteoporosis and fracture risk.

The study found a nonlinear relationship between PM_{10} and osteoporosis risk, which may be one of the reasons for the inconsistent findings between bone mineral density and osteoporosis.

Additionally, the inconsistent results between $PM_{2.5}$ and PM_{10} may be because $PM_{2.5}$ has a larger specific surface area compared to PM_{10} and can adsorb more compounds and metals, which could affect the balance of bone metabolism. Participants with low GRS and the highest air pollutant concentration had the highest risk of osteoporosis and fractures.

Finally, the researchers assessed the joint effect of APS and GRS on the risk of osteoporosis and found that participants with higher APS and lower GRS had a higher risk of developing osteoporosis and fracture.

In conclusion, this study performed a systemic study to disclose the associations between air pollution exposure and osteoporosis risk, and highlighted the combined effects of multiple air pollutants and their interaction effects with genetic factors on osteoporosis risk.

The findings emphasize that improving air quality can reduce the risk of developing osteoporosis and fracture, which has important implications for the development of environmental health policies.

Source: Frontiers in Public Health, Vol. 11, Article 1119774, March 2023.

Unexpected Air Pollutants with Potential Human Health Hazards

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nitrogen use efficiency of fertilizers and banned in Austria since 1993; biocides against insects (DEET and transfluthrin) used mainly outside agriculture; piperonyl butoxide (PBO), a synergist mixed into pesticide formulations; and four industrially used polychlorinated biphenyls (PCBs), long banned worldwide.

The city center showed the highest concentrations of biocides, PCBs and PBO, but also medium concentrations of nitrapyrin.

The potential human toxicity of the detected substances based on globally harmonized hazard classifications was high. Nitrapyrin was the most problematic of the eight substances detected in the samples, with statements for six hazard categories: Carcinogenicity, acute toxicity, specific target organ toxicity, skin irritation and sensitization, and eye irritation. DEET was the second most hazardous substance with four statements, PBO had three, PCBs had two, and transfluthrin had one human hazard statement.

The concentrations of the non-pesticide compounds in the current study were influenced mainly by meteorological parameters and only to a small extent by surrounding land use. Clearly, further research is needed to better understand how meteorological and application patterns interact.

Systematic monitoring of air and other media in conjunction with epidemiological assessments would be imperative to understand the effects of these substances on humans and the environment.

Source: Science of The Total Environment, Vol. 862, Article 160643, March 2023.

Toxicity Concerns and Biodegradation of Neonicotinoid Insecticides

Neonicotinoids (NEOs) are fourth generation pesticides, which emerged after carbamates, organophosphorus, and pyrethroid insecticides in 1980s. Today, NEOs are the most commonly applied insecticides globally, accounting for approximately 25% of all the pesticides. They are widely used in vegetables, fruits, cotton, rice, and other industrial crops to control insect pests. NEOs are considered ideal substitutes for highly toxic pesticides.

NEOs, including dinotefuran (DIN), athiamethoxam (THM), thiacloprid (THD), clothianidin (CLO), imidacloprid (IMI), nitenpyram, and cetamiprid (ACE), are synthetic compounds with a structure similar to that of nicotine.

Nicotinic acetylcholine receptor (nAChR) act as agonists and bind with acetylcholine receptors selectively, restricts insect acetylcholine (ACh), disturbs central nervous system leading to insect paralysis and death. Due to the unique mechanism of action, this type of insecticide does not have cross-resistance with conventional insecticides.

In addition, compared to traditional insecticides, NEOs are effective against a wide variety of insects, act at low concentrations, provide long-term control, have a systemic effect, can be applied using several methods, and have a high degree of crop safety.

NEOs are comparatively better than highly toxic organophosphorus pesticides, and cause less harm to the non-target organisms and environment. However, multiple studies have reported NEOs have harmful impacts on non-target biological targets, such as bees, aquatic animals, birds, mammals, and even human beings.

NEOs have been partially banned in Europe, but the use rate of NEOs is still high worldwide, which means that many non-target organisms are still exposed to insecticides.

The present review is focused on providing an in-depth understanding of neonicotinoid toxicity, microbial degradation, catabolic pathways, and information related to the remediation process of NEOs.

The current research on neonicotinoids shows that their toxic effects on non-target organisms vary between species. Among them, imidacloprid has the highest toxicity, and both dinotefuran and nitenpyram have lower toxicity.

It needs to be pointed out that the current experiments on neonicotinoids are mostly carried out in laboratories. Therefore, future research can consider the following aspects: (1) observing the toxic effects and mechanisms of a variety of NEO insecticides or combined exposure with other pesticides on different species of organisms, which are more in line with the exposure of organisms in the real environment; (2) combining a variety of analytical methods to study the toxic mechanism of NEO insecticides in different species to provide a standard for the future use of pesticides on the market; and (3) intensifying the research on vertebrates and model organisms to infer the effect on humans.

When using NEOs as a seed treatment or as granules, active ingredients partially (2-20%) enter the plants through root absorption whereas 80-98% remains in the soil, environment, or lost in planting, or eventually enter surface water or groundwater. These facts increase the risk of exposure to NEOs.

Therefore, there is an urgent need to develop an effective and sustainable approach for the on-site degradation of NEOs. At present, there are various methods for pesticide residual removal from the environment, including physical, chemical, and biological means.

The chemical and physical degradation techniques are costly, require harsh conditions, and may result in pollution.

Microbial degradation is a key natural method for eliminating neonicotinoid insecticides, as biodegradation is an effective, practical, and environmentally friendly strategy for the removal of pesticide residues.

To date, several neonicotinoid-degrading strains have been isolated from the environment, including *Stenotrophomonas maltophilia, Bacillus thuringiensis, Ensifer meliloti, Pseudomonas stutzeri, Variovorax boronicumulans,* and *Fusarium* sp., and their degradation properties have been investigated.

These microorganisms can convert NEOs into nontoxic or less toxic metabolites through various mechanisms and metabolic pathways. In addition, the synergistic effect of microbial communities on NEOs degradation requires further investigation. Finally, the study of functional genes and enzymes for microbial degradation is important to better understand the degradation mechanisms in polluted environments.

In the future, advanced technologies such as proteomics, metabonomics, and transcriptomics are needed to explore the missing links and molecular mechanisms and catalytic pathways involved in the process of biodegradation.

The recent advancements in high-throughput molecular and next-generation sequencing tools might ease the field applicability of neonicotinoid-degrading microbes from different contaminated areas.

Source: Environmental Research, Vol. 218, Article 114953, February 2023.

Prenatal PFAS Exposure and Early Childhood Neurodevelopment

Epidemiological studies have found that prenatal exposure to perfluoroalkyl and polyfluoroalkyl substances (PFAS) was associated with neurodevelopmental impairments in children, including executive function deficits, cognitive dysfunction, poor mental development, increased risk of neuropsychological problems, and even neurodevelopmental disorders.

The manufacturing of traditional long-chain PFAS, such as perfluoro-octane sulphonate (PFOS) and perfluorooctanoic acid (PFOA), is subject to global control due to their well-documented adverse effects on the environment and human health. Short-chain PFAS analogs (C4-C6), such as perfluorobutanoic acid (PFBA) and perfluorohexanesulfonic acid (PFHxS), as well as novel alternatives like chlorinated polyfluorooctane ether sulfonate (Cl-PFESA) have been widely used in industry to replace legacy long-chain PFAS.

Compared with long-chain PFAS, short-chain PFAS have lower bio-accumulation properties, but they have longer-distance migration potential. As a result, the health impacts of short-chain PFAS should be addressed.

PFAS can cross the placenta barrier and thus expose the fetus during the vulnerable period of development. Nowadays, individuals are regularly and simultaneously exposed to mixtures of PFAS. However, the joint effects of PFAS and their substitutes on neurodevelopment, particularly the neurodevelopmental trajectories, are rarely reported.

The present study was then conducted to assess prenatal exposure to single and mixture of PFAS and their effects on child neurodevelopment at 2, 6, 12, and 24 months of age based on a prospective birth cohort in China.

Children with relatively low scores from 2 to 24 months were classified into a low-score group and were used as a risk group in each domain.

PFOS, PFOA, PFHxS, and 6:2Cl-PFESA were detected in over 90 % samples which PFOA had the highest concentration.

The results showed that legacy long-chain PFAS (PFOA, PFOS, PFNA, and PFDA) were associated with declines in the communication domain, especially at 6 months of age. Short-chain PFAS (PFHxS) and novel alternatives (6:2Cl-PFESA) were also significantly associated with poor scores of the communication domain at 6 months of age.

PFOS, PFDA, PFHxS, and 6:2Cl-PFESA were associated with an increased risk of being in the low-score group in the early childhood communication domain's trajectory.

In addition, the gender-specific analysis found that boys may be more sensitive to legacy long-chain and short-chain PFAS. More evidence and systematic analysis are required to specify gender differences.

Each mixture quartile increment was associated with a 1.60 decrease in communication domain scores of 6-month-old infants, and with a 1.23-fold risk of being in the low-score group of the communication domain. The mixture effect was mainly attributed to PFOS.

This study is one of the most comprehensive studies to explore the effects of different kinds of PFAS, including legacy long-chain PFAS, short-chain PFAS, and novel PFAS alternatives, on neurodevelopment at multiple time points in early childhood.

In conclusion, exposure to legacy long-chain PFAS (PFOA, PFOS, PFNA, and PFDA), short-chain PFAS (PFHxS), and novel alternatives (6:2Cl-PFESA) were associated with an increased risk of impaired communication domain development, especially in boys, on basis of multiple PFAS and repeated neurodevelopment measurements.

PFOA, PFOS, and PFHxS can even affect the communication domain's trajectory throughout the whole infancy. The impacts of PFAS mixtures on the development of the communication domain were substantially greater than the effects induced by individual PFAS.

Source: Environment International, Vol. 173, Article 107850, March 2023.

Exposures to Organophosphate Flame Retardants and Amniogenesis: *In Vitro* Model

Organophosphate flame retardants (OPFRs) existed ubiquitously in building materials and various consumer products, such as mobile phones and baby products, and have therefore been detected in humans worldwide, including pregnant women and fetuses. Several epidemiological studies have associated OPFR exposure with biochemical miscarriage.

Biochemical miscarriage was defined as very early fetal loss, in which the initial serum or urine biochemical test is positive, but it does not progress into a clinical pregnancy. Approximately 75% pregnancies end up as biochemical miscarriage.

Moreover, human early pregnancy is a stage at which the blastocyst contacts and invades the maternal endometrium and the amniotic sac emerges from the embryonic inner cell mass by differentiating into squamous amniotic ectoderm.

Amniogenesis occurs during implantation and is one of the keystones for early human embryogenesis. Disrupted amniogenesis can lead to embryonic development failure and subsequent embryonic death at an early stage.

The fundamental role of amnio-genesis in early pregnancy led us to postulate that some OPFRs may also increase the risk of biochemical miscarriage by inhibiting this develop-mental process.

The present study was conducted to screen chemicals that may disrupt amniogenesis in an amniotic sac

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FAO: The Impact of Microplastics on the Gut Microbiome and Health - A Food Safety Perspective -

With a food safety focus, a scientific literature review on **the impact of microplastics on the gut microbiome and health** was conducted by the Food and Agriculture Organization (FAO) of the United Nations, to characterize the current understanding about the effects of microplastics on the gut microbiome and potential health implications.

The main aspects of analysed are (1) the effects of microplastics on the composition, diversity and function of gut microbiome using *in vitro* and *in vivo* models; (2) health implications resulting from the microplastic-microbiome interactions and underlying mechanisms; (3) the establishment of causality; and (4) influence of the gut microbiome on microplastic biodegradation.

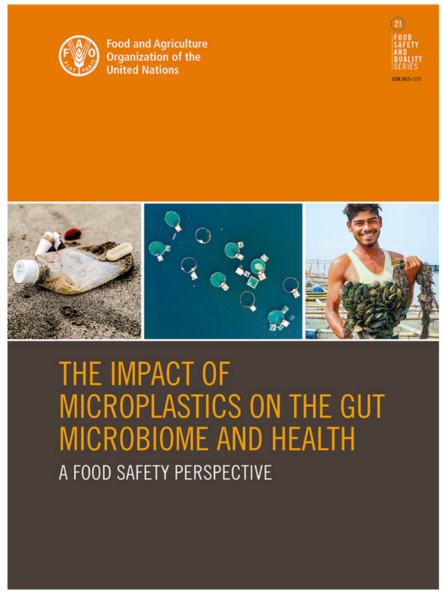
The gut microbiome is highly dynamic and complex microbial community that resides and interacts within the gastro-intestinal tract. This "community" can take part in various physiological activities, such as digestion and immune function, and helps maintain intestinal and systemic homeostasis.

In addition, the gut microbiome is very sensitive to environmental factors, including diet, which can have both positive and negative impacts on health. Imbalances of the gut microbiome have been associated with various disorders, including obesity, diabetes and inflammatory bowel disease.

A better understanding of how dietary components can impact the gut microbiome and human health is crucial for improving food safety risk assessment.

The research was also scoped to identify current gaps, limitations and needs for the eventual consideration of microbiome-related data in chemical risk assessment.

The outcomes will provide information which can be used to improve food safety policies.



Source: FAO. 2023. The impact of microplastics on the gut microbiome and health – A food safety perspective. Food Safety and Quality Series, No. 21. Rome.

Exposures to Organophosphate Flame Retardants and Amniogenesis: In Vitro Model

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embryoid model and to investigate the potential mechanism of amniogenesis failure, with a focus on OPFRs. This study developed a high-throughput toxicity screening assay based on transcriptional activity of octamer-binding transcription factor 4 (*Oct4*) which was one of the main pluripotency factors in early developmental stages.

Human amniotic sac embryoids can be derived from human embryonic stem cells, which provided a feasible approach to assess the toxicity of chemicals in human amniogenesis.

Eight positive hits exhibiting *Oct4* expression were identified, including five aryl-OPFRs, two alkyl-OPFRs, and one halogenated-OPFR, and 2-ethylhexyl-diphenyl phosphate (EHDPP) and isodecyl diphenyl phosphate (IDDPP) showing the strongest inhibitory activity. EHDPP and IDDPP were found to disrupt the rosette-like structure of the amniotic sac or inhibit its development.

Functional markers of squamous amniotic ectoderm and inner cell mass were also found disrupted in the EHDPP- and IDDPP-exposed embryoids.

Mechanistically, embryoids exposed to each chemical exhibited abnormal accumulation of phosphorylated nonmuscle myosin (p-MLC-II) and were able to bind to integrin β1 (ITGβ1).

Non-muscle myosin (MLC) was the major molecular driver in the intracellular actomyosin-dependent motility, and its activity was determined by p-MLC-II. In the OPFRs exposure groups, p-MLC-II was highly expressed in embryoids, ectopically clustered at the basal domain of the rosette but suppressed to localize at the apical domain. Thus, OPFRs may induce amniogenesis failure by accumulating p-MLC-II protein in the basal amniotic sac.

In summary, this study illustrated the adverse effects of OPFRs on human amniogenesis by inducing the ITGβ1-mediated abnormal accumulation of p-MLC-II in amniotic sac embryoids.

Although the determinants of biochemical miscarriage remain unclear, the study provides evidence for the association between early-life exposure to OPFRs and biochemical miscarriage.

The study nonetheless simulated a dynamic process of cavitation, which transformed embryonic discs into squamous amniotic ectoderms and demonstrated the impacts of OPFRs on amniogenesis failure in human amniotic sac embryoids.

This human embryonic stem cell (hESC)-based *in vitro* platform may facilitate the precise and rapid evaluation of industrial and consumer products that may induce biochemical miscarriage due to amniogenesis failure.

Source: Environmental Health Perspectives, Vol. 131, No. 4, Article 047007, April 2023.

CALENDAR OF EVENTS

International Training Courses at Chulabhorn Research Institute, Year 2023

	Training Course	Date	Duration	Closing Date
1	Environmental Toxicology and Health	June 27 – July 5, 2023	7 work days	May 5, 2023
2	Fundamentals of Environmental Immunotoxicology and Reproductive Toxicology	October 2 – 6, 2023	5 work days	August 21, 2023
3	Environmental and Health Risk Assessment and Management of Toxic Chemicals	November 27 – December 2, 2023	6 work days	October 16, 2023

Course Coordinator: *Khunying* Mathuros Ruchirawat, Ph.D.

Course Description:

Fundamentals of Environmental Immunotoxicology and Reproductive Toxicology (October 2 – 6, 2023)

The fundamentals course is an integration of science and policy, and covers the principals of human health and environmental risk assessment; the risk assessment paradigm; the risk assessment and management processes, which start from identification of the hazard, assessment methods, the mode of action and human relevance framework, the inherent uncertainties in each step, and the relationship between risk assessment and risk management, as well as the need for open, transparent and participatory acceptance procedures and credible communication methods. Emphasis will be placed on potential adverse health effects of human exposure to environmental hazards, although the principles of ecological risk assessment will also be covered. The course also teaches the application of risk assessment methods to various problems and describes the policy context in which decisions to manage environmental health risks are made. The applications of environmental impact assessment procedures for identifying and assessing risk are also covered. Importantly, the course teaches the practical application of risk assessment methods to various problems using case studies relevant to problems faced in developing countries.

Requirement: Participants should hold a bachelor's degree in chemistry, biological sciences or medicine and have at least two years of work experience and responsibilities related to the assessment of risk.

Fellowships:

A limited number of fellowships are available that will cover roundtrip airfare, accommodation (on site) and meals, training materials, and health insurance.

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More information and application:
Please visit - http://www.cri.or.th/en/ac_actcalendar.php

The ICEIT NEWSLETTER is published quarterly by the International Centre for Environmental and Industrial Toxicology of the Chulabhorn Research Institute. It is intended to be a source of information to create awareness of the problems caused by chemicals. However, the contents and views expressed in this newsletter do not necessarily represent the policies of ICEIT.

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