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Metal Toxicity and Alzheimer's Disease

Metals serve important roles in the human body, including the maintenance of cell structure, regulation of gene expression, antioxidant response, and neurotransmission.

There is a strong association between accidental metal exposure and various neurodegenerative disorders, including Alzheimer's disease (AD), the most common form of dementia that causes degeneration in the aged.

Neuropathological changes in the AD brain are linked to the aggregation of amyloid-β (Aβ) and the microtubule-associated tau protein in neurofibrillary tangles, leading to cognitive impairment of neuronal connectivity and neuron loss.

Aβ's structure and harmful effects in causing oxidative stress, autophagy, and neuroinflammation have been widely studied. The results suggest that Aβ aggregation is not the initial event in AD pathogenesis but rather a later event.

Chronic exposure to various metals is a well-known environmental risk factor that has become more widespread due to the rapid pace at which human activities are releasing large amounts of metals into the environment.

Consequently, humans are exposed to both biometals and heavy metals, affecting metal homeostasis at molecular and biological levels.

Homeostasis of key biometals such as calcium, magnesium, manganese, copper, zinc, and iron is disrupted in AD. Moreover, these metals play an important role in tau and Aβ metabolism and aggregation. It has been hypothesized that targeting metal interactions with Aβ may be effective in preventing AD.

This review highlights the effects of biometals and heavy metals on the brain, including how they contribute to AD and immune system dysregulation.

In addition, the findings confirm that the disruption of immune-related pathways is a significant toxicity mechanism through which metals may contribute to AD.

The association between biometal metabolism, genetic and environmental exposures, and the pathophysiology of neurodegenerative disorders merits additional exploration, particularly in the light of recent developments in metal neurobiology.

Metal ions are implicated in the majority of these degenerative disorders, making them a promising target for future therapeutic approaches. One strategy is to chelate and sequester the ions, limiting their ability to interfere with protein folding or prevent them from undergoing oxidative processes. Redistributing metal ions with newer approaches has therapeutic effects.

Metalloproteomics developments have contributed to improved knowledge of the mechanics and exact involvement of metalloenzymes and proteins in the brain.

Many drugs have recently been developed to reduce metal ions associated with both metal-induced Aβ aggregation and ROS generated by this and other aggregates through chelation.

Developing drugs with a multitargeted action may be the next step in treating neurodegenerative disorders such as AD, but they will need to be validated and evaluated further.

Source: Frontiers in Pharmacology, Vol. 13, Article 903099, August 2022.

Mercury Exposure and Risk of Type 2 Diabetes

Type 2 diabetes mellitus (T2DM) is a worldwide health concern. It is a multifactorial disease with different etiologies ranging from genetics to lifestyle and is linked to further complications such as cardiovascular and renal diseases, as well as mortality.

The effect that exposure to heavy metals can have on T2DM, obesity, and metabolic syndrome has been assessed previously.

Specifically, some metals such as cadmium (Cd), mercury (Hg), and metalloid arsenic (As) are hypothesized to be related to the incidence of T2DM. However, the available evidence is contradictory. The sources of these toxic metals are mainly contaminated water, polluted air, crops harvested in contaminated soil, dental care, fish consumption, and some industrial processes.

In general, Hg exposure has a broad range of toxic effects on cardiovascular, pulmonary, hematological, digestive, renal, immune, nervous, endocrine, and reproductive systems.

In relation to diabetes, Hg can target β-cells in the pancreas and induces dysfunction and apoptosis. Several mechanisms are considered such as altering Ca^{2+} homeostasis, activation of phosphatidylinositol 3-kinase (PI3K) Akt signaling pathway, and reactive oxygen species (ROS) production.

The present study is the first systematic review and meta-analysis which aimed to summarize the relationship between Hg levels in different body samples with the risk of T2DM.

Overall, the findings provide consistent epidemiological evidence that Hg levels in the blood and hair samples of T2DM patients were considerably higher than in the non-T2DM controls.

Nevertheless, the study revealed no significant association between Hg exposure and the risk of T2DM in the overall analysis and subgroup analysis based on the sample source (blood, urine, and toenail) and the type of study (case-control vs. prospective cohort).

The results of the gender-based analysis revealed that more exposure to Hg among the subgroup of men might be associated with a lower risk of T2DM, but not in women.

Additional studies are required to confirm this finding.

Source: International Journal of Clinical Practice, Vol. 2022, Article 7640227, September 2022.

Multi- and Transgenerational Effects of Environmental Toxicants on Reproduction

Declining human fertility has become a global public health priority during the past 30 years. Infertility affects nearly one in six couples worldwide (about 15% of couples in the reproductive age), with a progressive increasing incidence. The causes of male and female infertility are very heterogeneous.

Environmental toxicants (ETs) include several categories of compounds, very heterogeneous in their chemical structure and mechanism of action. Exposure to ETs induces reprotoxic effects by altering the production, maturation and quality of gametes and the reproductive cycle in both males and females, and the delivery and pregnancy outcomes and may determine premature reproductive senescence.

Among ETs, the endocrine-disrupting compounds (EDCs) encompass almost 800 different chemicals, including both natural and synthetic compounds, categorized into three major groups (i.e., pesticides, chemicals in consumer products and in food-contact materials). They alter the activation, synthesis, secretion and binding of endogenous physiological hormones, thus affecting several hormonal and metabolic processes.

In mammals, the exposure to ETs can affect both male and female fertility and their reproductive health through complex alterations that impact both gametogeneses, among other processes.

In humans, direct exposure to ETs concurs to the declining of fertility, and its transmission across generations has been recently proposed.

However, multi- and transgenera-tional inheritances of ET reprotoxicity have only been demonstrated in animals.

The recent studies performed on laboratory animal models investigating the effects of ETs, such as bisphenol A, phthalates, pesticides and persistent contaminants, on the reproductive system transmitted through generations.

The results clearly showed the impact of ETs on mammalian male and female gametogenesis, fertility and reproductive health.

In the males, they alter the correct spermatogenic process, the maturation of germ cells, induce apoptosis and azoospermia and decrease sperm motility. In the females, they mainly impair the correct progression of follicle maturation, induce follicle atresia and modify estrous cyclicity.

Overall, adult males are less affected than adult females poosibly because of the presence of spermatogonial stem cells in the testes leads to the continuous production of sperm, thus attenuating negative

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Air Pollution and Risk of Type 1 Diabetes

Despite multiple studies focusing on environmental factors conducive to the development of type 1 diabetes mellitus (T1DM), knowledge about the involvement of long-term exposure to air pollution seems insufficient.

Air pollution is a global environmental health risk that influences the onset and progression of a variety of health problems, including cardiovascular diseases, lung illnesses, cancer, and central nervous system disorders.

Particulate air pollution, which is primarily composed of organic and elemental carbon, metals, polycyclic aromatic hydrocarbons (PAHs), inorganic compounds, nitrates, sulfates, and other organic materials (such as polychlorinated biphenyls from industrial manufacturing), is a major component of air pollution and is of great research interest. There is mounting evidence that heavy metals adsorbed on PM are critical to its toxicity and negative health effects.

Particulate Matter (PM) e.g., $PM_{2.5}$ and PM_{10}, could be a carrier medium for a wide range of harmful pollutants, including heavy metals or PAHs.

Progressive environmental pollution is connected with a dynamic increase of T1DM incidences among children from different countries. An increasing number of studies confirm a negative relationship between endocrine disruptors and the occurrence of T1DM.

The main focus of epidemiological studies is placed on the relationship between exposure to various concentrations of particulate matter (PM_1, $PM_{2.5}$, PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) versus the risk of T1DM development. The effect of chemical air pollution on the risk of developing type 1 diabetes is summarized and discussed.

Nevertheless, air pollution is undoubtedly a factor attributing to premature deaths. The current review emphasizes on the risk of T1DM development associated with exposure to polluted air.

Knowledge of the health consequences of exposure to air pollution, including the presence of heavy metals, is still an important research problem requiring further examination.

An increasing number of studies confirm a negative relationship between endocrine disruptors and the occurrence of T1DM. Cadmium, arsenic, copper, mercury, manganese, and lead are documented to be endocrine disruptors. The exposure to selected heavy metals and the possible risk of developing type 1 diabetes are discussed.

Modern and more adequate methods for air pollution monitoring were also introduced, with a special emphasis on micro-sensors, mobile and unmanned measuring platforms, satellites, and innovative approaches of Internet of Things (IoT), 5G connections.

While the data about air pollution continues to grow worldwide with new technologies and more sensitive sensors, the association of the composition of air pollution with autoimmune diseases, such as T1DM, should also be explored in detail.

Although the specific molecular mechanism(s) behind the link between air pollution exposure and a higher risk of diabetes and metabolic dysfunction is yet unknown, the available data indicates air pollution-induced inflammation and oxidative stress as a significant pathway.

Improved understanding of environmental factors favorable to the development of different civilizational diseases, and autoimmunity, including T1DM, would be beneficial for further disease prevention, and implementation of emission control legislation.

Source: Antioxidants, Vol. 11, Issue 10, Article 1908, September 2022.

Multi- and Transgenerational Effects of Environmental Toxicants on Reproduction

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repercussions on male fertility. On the contrary, the fixed, nonrenewable pool of germ cells in the ovaries determines the major susceptibility of females to this category of compounds.

These alterations and the severity of the phenotype are not always directly related to the compound or to its exposure dose, suggesting the absence of a monotonic dose-response relationship.

Direct exposure during adulthood generates alterations that may be passed to children and then to grandchildren through epigenetic changes that occurred in the parents' germline.

Preconception exposure of F0 (ancestral) adult males or nonpregnant female germ cells gives birth to a F1 litter, which may be affected (multigenerational transmission). Although not directly exposed, the F2 generation may present ET-induced effects (transgenerational transmission).

These multi- and transgenerational inheritances may be mediated by epigenetic alterations, such as DNA methylation, histone tails and noncoding RNAs, which may play a mechanistic role in a nongenetic transmission of environmental information exposure through the germline across generations.

Another aspect that remains scarcely known is concerned with the effects exerted by ETs on the reproduction of wild mammalian populations, which might have negative impacts on the maintenance of the species.

Lastly, long-term follow-up studies in humans are needed to further investigate the association between exposure and the risk of reproductive dysfunctions throughout generations and for planning public health policies.

Source: Cells, Vol. 11, Issue 19, Article 3163, October 2022.

Environmental Substances Associated with Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a slowly developing non-communicable disease (NCD), causing non-reversible obstruction and leading to marked morbidity and mortality. Besides traditional risk factors such as smoking, some environmental substances can augment the risk of COPD.

It is difficult to indicate an epidemiological association between environmental chemical exposure and chronic diseases. In everyday life, humans are simultaneously exposed to small concentrations of various harmful environmental substances together with several other disease risk factors.

Developing COPD takes decades. It is not possible to evaluate the effect of each single factor in its pathogenesis. Air pollution (a mixed amount of chemical and biological pollutants) is associated with COPD in cellular and animal models. However, an epidemiological causal relationship between individual air pollutants and COPD has not been detected.

One of the most common methods for determining the phases of COPD is the Global Initiative for Chronic Obstructive Lung Disease (GOLD Staging System), consisting of four different stages using spirometry, as the forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC measurement, varying from mild to severe disease description.

The BODE Index (body mass, obstruction of airflow, dyspnea, and exercise capacity index) measures mortality risk for COPD and includes investigation of body mass, obstruction of airflow, dyspnea (difficulty of breathing), and exercise capacity, and it is used to understand the prognosis and severity of the symptoms.

The European Human Biomonitoring Initiative (HBM4EU) is a combined project including 30 countries (26 European Member States, three associated countries, and Switzerland), the European Environment Agency, and the European Commission, co-funded under Horizon 2020.

The primary objectives of the HBM4EU are to evaluate human exposure to chemicals and create knowledge on chemical exposure and its health impacts within populations with the help of human biomonitoring (HBM). Within the HBM4EU, eighteen priority substances or substance groups were chosen.

This scoping review presents specific HBM4EU priority substances and substance groups having an association or a possible association with COPD. It also describes the possible causes of chemical exposure and how these exposures are assessed in humans.

Seven of these substances or substance groups are reported to have an association or a possible association with COPD.

Pesticides in general and especially organophosphate and carbamate insecticides, and some herbicides, lead (Pb), and polycyclic aromatic hydrocarbons (PAHs) showed an association with COPD, chronic bronchitis, and/or decreased lung function. Cadmium (Cd), chromium (Cr and CrVI), arsenic (As), and diisocyanates, showed a possible association.

As and diisocyanates were more strongly associated with decreased lung function and respiratory symptoms than COPD per se. Occupational exposure was prevalent especially regarding pesticides, and to some extent regarding Pb and PAHs.

Main exposure routes, vulnerable and high-exposure risk groups, and matrices where these substances are measured are described.

According to the review, there is evidence of negative effects on lung function related to environmental and occupational chemical exposures. In real life, people are exposed to various substances at the same time, and it is difficult to determine the role of a single substance.

In epidemiological studies, an inverse association was observed between lung function parameters and levels of specific environmental substances in the measurement matrices.

COPD diagnosis in spirometry is a difficult endpoint. However, spiro graphic modifications are essential in diagnosing COPD. Typically, the diagnosis is established late in the conditions in which it is known that the pathophysiological changes develop slowly. It is noteworthy that if lung function parameters (FVC and FEV_1) are in decline (maybe already in childhood), this may lead to a later diagnosis of COPD or other respiratory diseases.

Due to long latency in the COPD disease process, the role of chemical exposure as a risk factor for COPD is probably underestimated. Therefore, research should be extended to gain a better knowledge of the harmful effects of chemical exposure in the development of specific lung diseases.

The combined impacts of different environmental substances on human health have been scarcely studied, although people are increasingly exposed to various substances. Therefore, joint assessment of the adverse effects is promptly required.

More research is needed to support evidence-based conclusions. Generally, chemical exposure is a growing issue of concern, and prompt action is needed to safeguard public health.

Source: International Journal of Environmental Research and Public Health, Vol. 19, issue 7, Article 3945, March 2022.

Chronic Exposure to Deltamethrin Induces Cardiac Injury

Deltamethrin, a type II synthetic pyrethroid pesticide with a cyano group in the molecular configuration, is widely employed in veterinary medicine and farming, owing to its low residue and toxicity, and great efficiency.

Since an increasing numbers of ecotoxicological studies related to complex toxicological syndromes induced by deltamethrin, exploring the deltamethrin-induced toxicity mechanism becomes necessary. Multiple tissues and organs were grievously damaged by the interference of deltamethrin, i.e. liver, brain, and testis. Few studies investigate the chronic deltamethrin-induced underlying effects on the heart.

Growing evidence indicates that deltamethrin-induced non-target toxicity most likely tightly related to excessive oxidative stress. Oxidative stress is often accompanied by the generation of a great quantity of reactive nitrogen species (RNS) and reactive oxygen species (ROS).

The heart is vulnerable to oxidative stress due to its specialized structure, and has the highest rate of production of ROS and lower levels of antioxidants and total activity of antioxidant enzymes.

It is well-known that nuclear factor erythroid-2-related factor 2/ heme oxygenase-1 (Nrf2/HO-1), a pivotal endogenous anti-oxidative pathway, acts on inhibiting oxidative stress-induced cell injury under the activated state.

Nrf2 is a critical anti-oxidant stress factor in cells, which has a variety of downstream targets for cell protection. Functionally, Nrf2 can inhibit apoptosis, regulate autophagy, reduce inflammation, and ameliorate endoplasmic reticulum stress by regulating phase II detoxification enzyme. The most susceptible and extensively researched enzyme, HO-1, assisted in modulating rise oxidative stress and preserving redox state in many biological environments as a rate-limiting enzyme involved in metabolism of heme.

Organisms are also able to up-regulate the Nrf2/HO-1 signal axis to increase Nrf2 and HO-1 expression, which in turn effectively ameliorates cardiomyocyte apoptosis and reduces the range of infarction and ischemia in myocardial tissue.

The present study was devised to identify the effect of deltamethrin exposure on oxidative stress in quail cardiomyocytes and explores the latent mechanism of deltamethrin-induced cardiac injury based on the Nrf2/HO-1 pathway.

In this study, quails were established as a cardiac injury model through gastric infusion of various doses of deltamethrin (0, 15, 30, and 45 mg/kg b.w.) for 12 weeks.

The results showed that deltamethrin could induce cardio-myocyte injury in a dose-dependent manner through weakening anti-oxidant defense via down-regulating Nrf2 and its downstream protein HO-1.

Stimulation of deltamethrin induced apoptosis in quail heart by decreasing the protein expressions of B-cell lymphoma-extra large and B-cell lymphoma gene 2 (Bcl-2), as well as increasing P53, caspase 3, and Bcl-2-associated X (Bax) protein levels.

Oxidative stress accelerates p53 activation, and activated p53 triggers multiple signaling pathways leading to cell cycle arrest, and the apoptosis of cells. The migration of anti-apoptotic proteins (Bcl-xl, Bcl-2) results in cell survival, whereas, the increased pro-apoptotic protein Bax induces apoptosis.

Meanwhile, relative levels of nuclear factor-kappa B (NF-κB) and interleukin-1β (IL-1β) in quail hearts were up-regulated under deltamethrin intervention progressively.

NF-κB is stimulated by pro-inflammatory cytokines, then activated and translocated to the nucleus. Subsequently, NF-κB accumulates in the nucleus and then enhances the generation of proinflammatory cytokines, such as IL-1β and TNF-α. In turn, TNF-α and IL-1β collectively regulate the activation of NF-κB through positive feedback adjustment. NF-κB can further aggravate apoptosis with the activation of the pro-apoptotic protein Bax.

As the downstream protein of Nrf2, HO-1 can inhibit the up-regulation of Bax and attenuate apoptosis, and can also alleviate apoptosis by inhibiting the production of ROS via the pathway mediated by mitochondria.

The results indicate that deltamethrin promotes NF-κB nuclear displacement and IL-1β production via inhibiting the Nrf2/HO-1 pathway. Consequently, deltamethrin can up-regulate inflammatory cytokines in the organism and mediate the apoptosis of cardiomyocytes by inhibiting the Nrf2/HO-1 signaling pathway.

In summary, the present study provides evidence that deltamethrin promotes cardiomyocyte inflammation and apoptosis through inhibiting the Nrf2/HO-1 signaling pathway. Regulation of Nrf2/HO-1 pathway may be an effective therapeutic approach for deltamethrin-induced cardiac injury. Meanwhile, our research could provide a theoretical basis to further explore the health risks stimulated by hazardous pesticides.

Source: Chemosphere, Vol. 300, Article 134479, August 2022.

WHO - Parkinson Disease: A Public Health Approach Technical Brief

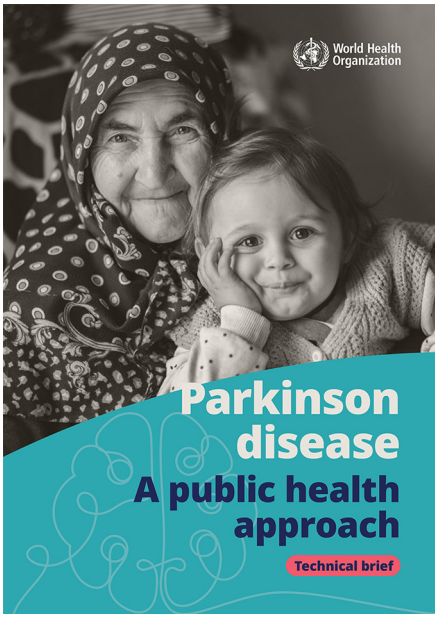
The technical brief entitled "**Parkinson disease: A public health approach**" outlines the global burden, treatment gaps and crucial areas for actions for Parkinson disease (PD) and provides considerations for policies, implementation and research with a focus on low- and middle-income countries.

PD is a degenerative condition of the brain associated with motor symptoms (slow movement, tremor, rigidity, and walking imbalance) and a wide variety of non-motor complications (cognitive impairment, mental health disorders, pain and other sensory disturbances). Motor impairments, including involuntary movements (dyskinesias) and painful involuntary muscle contractions (dystonias) contribute to limitations in speech, mobility and thus restrictions in many areas of life. Progression of these symptoms and complications markedly decrease function and quality of life which result in high rates of disability and care requirements as well as stress and burden of carers.

Globally, the prevalence of PD has doubled in the past 25 years with global estimates in 2019 showing over 8.5 million individuals living with PD. Disability and death due to PD are increasing faster than for any other neurological disorder. Current estimates suggest that, in 2019, PD resulted in 5.8 million disability-adjusted life years, an increase of 81% since 2000, and caused 329,000 deaths, an increase of over 100% since 2000.

Despite the significant impact of PD, there is inequality in the availability of resources and services to provide treatment and care especially in low- and middle-income countries.

The technical brief on PD is targeted to policy-makers, health programme managers and planners, health-care providers, researchers, people with PD and their carers, and will support the implementation of the intersectoral action plan on epilepsy and other neurological disorders.



Source: WHO. Parkinson Disease: A Public Health Approach: Technical Brief. June 2022. (https://www.who.int/publications/i/item/9789240050983)

Prenatal Co-Exposure to Metals (Pb, Hg, and Mn) and Neurodevelopment in Children during the First Year of Life

Lead (Pb) and mercury (Hg) are classified by the World Health Organization (WHO) among the ten chemicals of major public health concern because they are widespread environmental pollutants known to be neurotoxic at relatively low doses during early stages of development.

Manganese (Mn) can also be neurotoxic, but unlike Pb and Hg, it is an essential element. Therefore, both a Mn-deficient diet and excessive Mn environmental exposure may affect neurodevelopment.

Real-life exposures usually consist of simultaneous contact with multiple combinations of different levels of several pollutants that might produce synergistic or antagonistic effects. The chemical mixtures and their health effects vary among countries, according to demographics, socio-economic factors, and urban and industrial development.

Furthermore, relatively low concentrations of a metal that have not been associated with an adverse effect might be contributing to one in the presence of other neurotoxic metals.

Neurodevelopmental processes during early life stages are at their peak, and many environmental pollutants are not blocked by the placenta or the blood-brain barrier, hence causing structural and functional damage to the brain that can affect immediate and/or later-life health outcomes.

Throughout pregnancy, the placenta actively or passively transports elements that are essential, although potentially toxic at certain levels (such as Mn), and purely toxic elements (such as Pb and Hg) and these elements can accumulate in fetal tissues such as the brain.

The present study investigated whether concurrent *in utero* exposure to background Pb, Hg, and Mn was associated with language, cognitive, and motor neurodevelopment indices in boys and girls in Mexico during their first year of life.

Maternal mean blood levels (μg/L) during the third trimester of pregnancy were Pb = 11.2, Hg = 2.1, and Mn = 10.2.

Mean language, cognitive, and motor development scores of the infants at each age were between low-average and average. The results showed an apparent declining tendency in the language scale as age increased during the first year of life, but not in the motor and cognitive scales.

The results showed that language development coefficients of the offspring

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The Chem HelpDesk

"Strengthening capabilities for sound chemicals management"

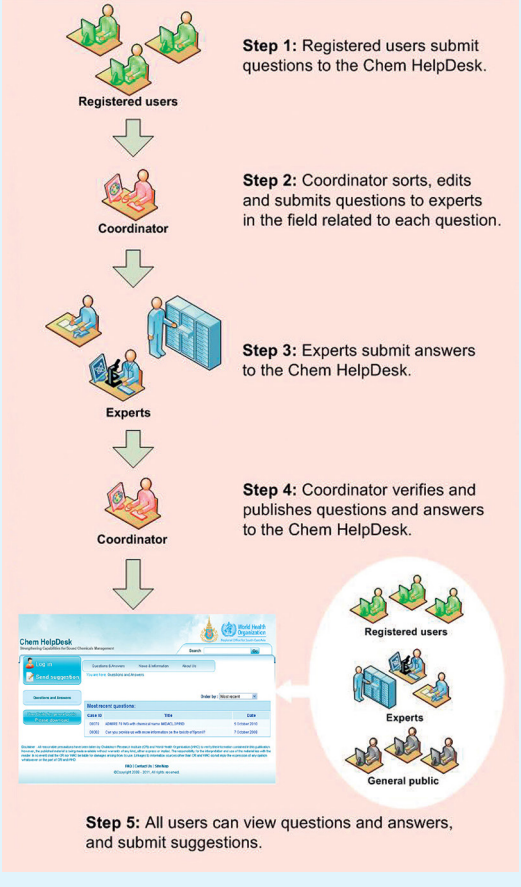
The Regional HelpDesk for Chemical Safety, or **Chem HelpDesk** was established as a joint-initiative between WHO SEARO and CRI, through the WHO Collaborating Center for Capacity Building and Research in Environmental Health Science and Toxicology. The aims of the Chem HelpDesk are to address the issue of the widening gap in the fields of chemical safety and chemicals management between developed and developing countries, and to empower countries in the South-East Asia Region to manage the import, manufacture and processing, storage, distribution, transport, use, recycling and disposal of chemicals, in ways that minimize significant adverse impacts on health and the environment.

The Chem HelpDesk is not-for-profit, and through its website provides cost-free answers to questions submitted by registered users. These answers are provided by experts in the respective fields, who supply technical and scientific advice as part of a Community of Practice (CoP). It is the aim of the Chem HelpDesk to benefit users and to help countries in areas of most need to protect human health and the environment through the safe use and management of chemicals.

In addition to the **"Questions & Answers"** service for registered users, the website also provides information on the safe use of chemicals, as well as a comprehensive list of links to other important websites related to chemicals management in the region. General users have access to the database of questions and answers, as well as all other information on the website.

For more information, please visit: http://www.chemhelpdesk.org
or e-mail: coordinator@chemhelpdesk.org

The functional workflow of the Chem HelpDesk is divided into 5 steps:



Prenatal Co-Exposure to Metals (Pb, Hg, and Mn) and Neurodevelopment in Children during the First Year of Life

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decreased by 1.5 points per 1 μg/dL increase in maternal blood Pb levels; the magnitude of the association increased in children with maternal blood Mn < 9.6 μg/L or Hg > 1.9 μg/L.

In conclusion, prenatal exposure to low Pb levels, resulting in maternal blood levels well below the current Mexico and US reference values (5 and 3.5 μg/dL, respectively), may impair the offspring's neurodevelopment during the first year of life.

The effect is especially evident in language development, and even more so if the pregnant women are also exposed to low levels of Hg, or apparently, if they are deficient in essential nutrients such as Mn.

This is important considering that most of the burden of disease of Pb, Hg, and Mn will be in scenarios of low-level exposures.

The co-existence in pregnant women of micronutrient deficiency and exposure to low background levels of Pb and Hg is not uncommon, especially in developing countries. However, these conditions are preventable, albeit especially challenging where they are most prevalent.

The results contribute to a better understanding of real-life susceptibility factors regarding the negative association of metals and neurodevelopment: timing, co-exposures, and perhaps nutritional circumstances.

Further research is required to characterize the dose-response curve of the co-exposure associations at other levels and to investigate if the associations found hold after the first year of life.

Source: International Journal of Environmental Research and Public Health, Vol. 19, No. 20, Article 13020, October 2022.

Residential Exposure to Airborne Polychlorinated Biphenyls and Cancer Risk

Polychlorinated biphenyls (PCBs) are classified as "Carcinogenic to Humans" by the International Agency for Research on Cancer (IARC), based on sufficient evidence for malignant melanoma and limited evidence for non-Hodgkin lymphoma (NHL) and breast cancer.

This classification is mainly based on studies of higher-chlorinated PCBs (HC-PCBs) typically found in food, rather than the lower-chlorinated PCBs (LC-PCBs) dominating indoor air in contaminated buildings.

Studies of HC-PCBs may not, however, be directly used for risk assessment of LC-PCBs, due to potential differences in mechanism of action. Carcinogenesis of HC-PCBs is mostly driven by dioxin-like PCBs through aryl hydrocarbon receptor (AhR) activation, whereas the mostly nondioxin-like LC-PCBs act through AhR-independent pathways, probably through metabolic activation and metabolites.

No previous human studies that have investigated cancer risk following exposure to LC-PCBs in indoor air specifically. Occupational studies of high PCB exposure mainly through inhalation do not indicate higher risk of malignant melanoma, NHL, and breast cancer but find indications of higher mortality from liver, gall bladder, and biliary tract cancers, although based on small numbers.

Animal studies support a carcinogenic effect of LC-PCBs in the liver, suggesting that exposure to airborne PCBs (predominantly LC-PCBs) may be associated with cancer in other organs than foodborne PCBs (primarily HC-PCBs).

The present study aimed to determine cancer risk following airborne PCB exposure in the Health Effects of PCBs in Indoor Air (HESPAIR) cohort of residents of two partly PCB-contaminated residential areas. Cancers previously associated with PCB exposure were of a priori interest, namely malignant melanoma, NHL, breast, liver, gall bladder, and biliary tract cancer.

This is the first population-based cohort study of residential exposure to airborne PCBs.

The study found no association between exposure to PCBs in indoor air in private homes and the risk for most of the specific cancers.

Higher risks of liver cancer and meningiomas (primarily benign) among residents in PCB-contaminated apartments were observed with indication of an exposure-response relationship.

Higher risks of pancreatic and testis cancers were suggestive, but effect estimates were inconsistent. Previously observed associations between HC-PCBs and malignant melanoma, NHL, and breast cancer were not confirmed.

The study did not confirm the previously reported higher risk of gall bladder and biliary tract cancer observed in PCB-exposed workers, but case numbers were small.

The present study examines the overall effect of airborne PCBs but not of specific LC-PCBs, because their concentrations are highly correlated. Further, because LC-PCBs are more easily metabolized and may act through their metabolites, serum measurements of parent congeners may underestimate the actual risk of LC-PCBs.

Although differences between contaminated and reference apartments in air and serum samples in a subset of ~200 residents were mostly attributed to LC-PCBs, the serum showed significantly elevated levels of some HC-PCBs among exposed residents, meaning that HC-PCBs or an interaction between HC- and LC-PCBs may contribute to observed associations.

In conclusion, residents exposed to airborne PCBs in their private homes had higher risk of liver cancer and meningiomas, although the risk for the majority of cancers was not higher.

The findings suggest a potential carcinogenic effect of LC-PCBs that is different from that of HC-PCBs. Even larger cohort studies, with biologically measured LC-PCBs and their metabolites, are warranted to enable firm conclusions about the potential human carcinogenicity of airborne LC-PCBs.

Source: Environmental Health Perspectives, Vol. 130, No. 10, October 2022.

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