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# Chulabhorn Research Institute

# 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".

## Her Royal Highness Princess Chulabhorn Receives the 2020 Grand Prix de la Charte Award from the Institut International de Cancerologie de Paris

***Monday February 3rd, 2020***
***at Chapelle Royale, Chateau de Versailles, France***


**Her Royal Highness Princess Chulabhorn Krom Phra Srisavangavadhana, President of the Chulabhorn Research Institute (CRI), Bangkok, Thailand, received the 2020 Grand Prix de la Charte award from the Institut International de Cancerologie de Paris** at a ceremony held at the Chapelle Royale, Chateau de Versailles on Monday February 3rd, 2020.

The Charter of Paris Against Cancer was established in 2000 by former French President Jacques Chirac and UNESCO Director Koichiro Matsuura. Her Royal Highness Princess Chulabhorn also took part in the signing of the charter in the World Summit Against Cancer in 2000, with the main objectives being improving care and services for cancer patients appropriate with human rights, promoting research for cancer therapy and prevention, and increasing public awareness on cancer. This award ceremony is organized annually to recognize distinguished individuals who work on this important global health issue.

Cancer is now the leading cause of death worldwide, with a complex etiology that makes diagnosis difficult. World health authorities have therefore made it a focus of sustained global efforts.

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# CRI's WHO COLLABORATING CENTRE ON CAPACITY BUILDING & RESEARCH IN ENVIRONMENTAL HEALTH SCIENCE & TOXICOLOGY

***Official Visit of Her Royal Highness Princess Chulabhorn Krom Phra Srisavangavadhana, President of the Chulabhorn Research Institute to the World Health Organization's Regional Office for South-East Asia***


On February 18th, 2020, Her Royal Highness Princess Chulabhorn Krom Phra Srisavangavadhana, President of the Chulabhorn Research Institute (CRI), led a team of senior researchers on an official visit to the World Health Organization's Regional Office for South-East Asia (WHO SEARO) in New Delhi, India, to review progress and next steps for the work carried out under the collaborative workplan between CRI and WHO. The workplan for this 4th term of CRI's WHO Collaborating Centre for Capacity Building and Research in Environmental Health Science and Toxicology, which was agreed in January 2018, is currently at the midpoint of the collaboration period.

CRI's International Centre for Environmental Health and Toxicology (ICEHT) has been a WHO Collaborating Centre for Capacity Building and Research in Environmental Health Science and Toxicology since 2005, with the following Terms of Reference: to promote and assist capacity-building activities and awareness in environmental/occupational health, toxicology and risk assessment; to promote and conduct collaborative research in environmental health science, particularly as it relates to emerging national and international problems and in vulnerable groups such as children; to establish and maintain linkages with relevant centres, particularly in the South-East and Western Pacific regions of WHO; and to act as a Regional Centre for Training in Chemical Safety.

The technical discussions covered three key areas: (1) capacity building and training, (2) information, education and communication, and (3) collaborative research.

Progress on capacity building and training included 7 Face-to-Face training courses at CRI in Bangkok with over 100 participants from 21 countries, the e-learning tool launched at SEARO in 2014 reaching 445 users, and a new module for the e-learning tool completed on risk assessment for chemical incidents in collaboration with WHO CC in Cardiff.

In terms of information, education and communication, CRI has become a part of the Steering Group on capacity building under new WHO Chemical Risk Assessment Network. CRI has taken over hosting and development of the Risk Train database for post- and undergraduate, continuing education, and not-for-profit training courses related to human health chemical risk assessment, and continued the development of Chemical Helpdesk to strengthen its relevance for networking and sharing of information on policies, regulations and contacts in Member States, with almost 300 news articles added in the past year.

In terms of collaborative research, CRI has shared research findings and methodologies developed by CRI research on vulnerable populations, e.g. air pollution and school children, e-waste recycling; and jointly-hosted the Asia-Pacific Conference on Children's Environmental Health in May 2018 with the US NIEHS to explore policy relevant research collaborations. From October 30th to November 1st, 2018, WHO organized the First WHO Global Conference on Air Pollution and Health at which Her Royal Highness Princess Chulabhorn addressed the conference to advocate for greater action to protect health. CRI also hosted the WHO SEARO Regional Workshop on Air Pollution and Health in June 2018, with the outcomes presented at the aforementioned Global Conference.

The key collaborations between CRI's WHO CC and WHO planned for the following year include:

(1) involvement of maternal and child health and environmental health focal points in the upcoming International Conference on Children's Environmental Health (tentatively set for early 2021) as a key bridge in moving from research to policy;

(2) dissemination of WHO training modules on Children's Environmental Health e.g., consider using in CRI training events and/or development of online courses;

(3) finalization of arrangements for hosting and maintenance of the RiskTrain database to assist capacity building efforts of the WHO Risk Assessment Network - this includes a survey of former students from CRI training courses to explore how to develop alumni of fellows and expand community of trainers;

(4) provide assistance in assessment of training needs and capacity, including laboratory facilities, in Myanmar prior to development of a training programme for 2021; and

(5) development of potential WHO-CRI collaborative activities on air pollution, including participation in a planned WHO SEA Regional Meeting on accelerating action on air pollution in cities (tentatively set for June 16-18th, 2020), particularly to share experience of linking air pollution monitoring data with health surveillance.

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## *Her Royal Highness Princess Chulabhorn Receives the 2020 Grand Prix de la Charte Award from the Institut International de Cancerologie de Paris Monday February 3rd, 2020 at Chapelle Royale, Chateau de Versailles, France*

*(Continued from page 1)*

Her Royal Highness Princess Chulabhorn Krom Phra Srisavangavadhana is recognized for her work in the area of cancer. She has long given importance to the study and research on cancer etiology, contributing factors specific to the local conditions, and molecular mechanisms of action towards improving cancer therapy.

Her Royal Highness Princess Chulabhorn established CRI in 1987 with cancer research as one of the focus areas, and later established the Chulabhorn Cancer Center (later renamed the Chulabhorn Hospital) for treatment of cancer using the latest methods and technologies, bringing these treatment opportunities to people who would otherwise not have access to them. Her Royal Highness Princess Chulabhorn has also focused her efforts on cancers prevalent in Thailand through collaborations with various international expert organizations.

The project entitled, **"Thailand's Initiative on Genomics and Expression Research for Liver Cancer or TIGER-LC"** in collaboration with the US National Cancer Institute, which pools expertise from a number of Thai institutions has been implemented.

Researchers of the consortium identified common molecular subtypes among Thai hepatocellular carcinoma and cholangiocarcinoma patients that linked to survival outcome. These subtypes have been observed in liver cancer patients of Asian descent, but not in patients of European descent, suggesting that common molecular subtypes are related to race/ethnicity. Subtype-related cancer drivers could improve early diagnostic and therapy allowing successful patient care with an outlook toward precision medicine.

Through this and countless other projects and activities through the years, Her Royal Highness Princess Chulabhorn has demonstrated a determination to continue research and to improve therapy for cancer patients, a key contribution towards improving public health in the country and region.

## *CRI's WHO Collaborating Centre on Capacity Building & Research in Environmental Health Science and Toxicology*

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**The organized courses in 2020 include:**

| | Training Course | Time |
|---|---|---|
| 1 | Principles of Toxicology, Toxicity Testing and Safety Evaluation | 14 January - 7 February 2020 |
| 2 | Detection of Environmental Pollutants and Monitoring of Health Effects | 24 February - 6 March 2020 |
| 3 | Environmental Toxicology | Canceled due to coronavirus outbreak |
| 4 | Environmental and Health Risk Assessment and Management of Toxic Chemicals | November - December 2020 |

Those who are interested in applying for a fellowship to attend CRI training courses in the areas of Environmental Toxicology, Environmental Health, and Risk Assessment and Risk Management of Toxic Chemicals can check the calendar of events on CRI's website at http://www.cri.or.th/en/ac_actcalendar.php.

# Effects of Ambient Particulate Matter on Fasting Blood Glucose: A Systematic Review and Meta-analysis

Diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Approximately 451 million adults worldwide had diabetes in 2017, and this number is expected to rise to 693 million by 2045.

Established risk factors include a family history of diabetes mellitus, age, obesity, and physical inactivity. Recently, however, particulate matter (PM) already defined as a major contributor to the global burden of disease, has recently been linked to diabetes, as well.

Fasting glucose, which is used to define diabetes, is also considered an indicator for prediabetes.

Since 2010, several population-based studies have found that ambient PM exposure has a negative influence on fasting blood glucose levels. However, these studies were conducted in a limited number of countries, and the results were not consistent.

A systematic review and meta-analysis was conducted to determine the relationship between $PM_{10}$, $PM_{2.5}$ and fasting blood glucose.

The studies were divided into groups according to PM size fractions ($PM_{10}$ and $PM_{2.5}$) and length of exposure. Long-term exposures were based on annual average concentrations. Short-term exposures lasted less than 28 days.

The review showed that elevated fasting blood glucose was statistically associated both with long-term exposure to $PM_{10}$ and $PM_{2.5}$ and with short-term exposure to $PM_{2.5}$.

Conclusions regarding exposure assessments, exposure time windows, susceptible populations and possible mechanisms were discussed.

Machine learning algorithms, such as random forest models, have been very popular due to their high performance in estimating air pollutant concentrations, especially in studies focusing on long periods of time and large research areas.

Researchers should select appropriate exposure assessment methods in light of their study's purpose. Different exposure assessment methods impact the reported outcomes.

Furthermore, various periods of exposure, lags and the lack of a time-activity mode will also increase exposure bias. Given the rapid increase in articles on this theme, it may become possible in the future to assess the effects of the exposure assessment method, exposure periods and lags.

Considering the necessity and the limitations imposed on current research, many more longitudinal studies that can confirm the causal relationship between ambient PM exposure and glucose levels should be carried out.

By using statistical methods such as machine learning or monitoring pollutants at the personal exposure level, an exposure assessment method with strong comparability and accuracy can be established to enhance our understanding of the relationship between PM exposure and blood glucose levels.

Further analyses of glucose parameters that consider study aims, populations and exposure durations are also needed. More studies focusing on varied populations should be conducted in the future to verify whether specific populations are particularly sensitive to PM exposure effects.

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***Source:*** Environmental Pollution, Vol. 258, Article 113589, March 2020.

# Cardiovascular Effects of Airborne Particulate Matter: A Review of Rodent Model Studies

In recent years, animal models have been growingly used to increase our knowledge about the toxicity of Particulate matter (PM) and the underlying mechanisms which leads to cardiovascular disease.

PM is a mixture of different elements and compounds, normally defined and classified by its aerodynamic diameter. The smaller fractions of particles can easily penetrate the respiratory tract and lung with damaging health consequences. This smaller fractions can also enter the circulatory system, affecting many organs such as the heart and brain, and the vascular system, etc.

In addition to diameter, chemical composition, surface area and other characteristics of PM influence its toxicity. Comparisons of various studies suggest that, while these particles may have different characteristics, PM is usually studied based on mass.

Many epidemiological studies showed clearly that short- and long-term exposures to airborne PM are associated with cardiovascular effects in humans. These adverse health effects may include ischemic heart disease (IHD), myocardial infarction (MI), arrhythmia, thrombosis, atherosclerosis, etc.

Recognizing that the systemic inflammation caused by circulatory levels of inflammatory cytokines triggers many cardiovascular effects, the number of studies investigating the toxicology of PM and mechanisms of cardiovascular effects in animal models, especially in rodents, has increased.

This article is a review of the current state of knowledge and findings of studies that have investigated the systemic inflammation and cardiovascular effects of PM in rodent models.

The six main areas covered in this review include: I) the nature of PM and toxicity mechanisms, II) systemic

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# Prenatal Exposure to Air Pollution as a Potential Risk Factor for Autism and ADHD

Genetic and environmental factors both contribute to the development of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). Environmental determinants alone may account for 10-40% of the risk for ADHD and around 40% for autism.

In this regard the impact of air pollution, recognized by the World Health Organization (WHO) as one of the biggest health threats of our time, can hardly be exaggerated. This particular environmental hazard may affect the central nervous system, making it a potential risk factor for developing ASD and ADHD. However, our understanding of its effects, especially in low-exposure areas, is limited.

Recent epidemiological studies have found associations between exposure to air pollution and an elevated risk of developing ASD in the United States, Taiwan, and Israel. However, these findings have not been reproduced in most European cohort studies investigating prenatal air pollution and autistic traits or ASD.

The present study investigated risks for ASD and ADHD associated with prenatal exposure to air pollution in areas with air pollution levels generally well below WHO air quality guidelines. The goal was to perform a population-based research to obtain high quality data on ASD and ADHD.

Air pollution concentrations were gauged with high spatial resolution, and potential confounders, such as other neuro-developmental disorders, perinatal factors, and socioeconomic status (SES) were identified from nation-wide registers.

The study used an epidemiological database (MAPSS) consisting of virtually all (99%) children born between 1999 and 2009 (48,571 births) in southern Sweden.

The study used Nitrogen oxide (NOx), a well-known marker for near-roadway exposure to air pollutants or ultrafine particles, to assess exposure.

Positive associations between air pollution exposure during the prenatal period and an increased risk of developing ASD were found in this longitudinal cohort study, but no similar associations were confirmed between air pollution and the risk of developing ADHD.

This study contributes to the growing evidence of a link between prenatal exposure to air pollution and ASD. It suggests that prenatal exposure, even below current WHO air quality guidelines, may increase the risk of ASD.

Autism can have a significant influence on both the individual's and family's wellbeing and on their future economic stability and productivity.

It has been postulated that if air pollution impairs children's health, ability to learn, and potential to contribute to society, further segregation between communities will occur. The environment is of special importance to the unborn child, which is vulnerable even as it undergoes rapid neurodevelopment.

Today, bold policies and new technology are lowering harmful emissions, decreasing average exposure levels, and contributing to a safer environment for all children.

Scientific evidence has shown that interventions to lower emissions can benefit children's neurodevelopment. More studies on possible preventive measures, both on the individual and the collective level, are urgently needed.

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***Source:*** Environment International, Vol. 133, Article 105149, December 2019.

## *Cardiovascular Effects of Airborne Particulate Matter: A Review of Rodent Model Studies*

*(Continued from page 4)*

inflammation, III) heart rate and heart rate variability, IV) histopathological effects, V) atherosclerosis, VI) thrombosis, and VI) myocardial infarction.

The studies were selected for review according to their relevance, meaningfulness, importance, and validity as they attempted to gather evidence from several types of PM, doses, and means of exposure.

This review shows that animal model studies have been successful in bringing new insights regarding mechanisms underlying PM-induced cardiovascular diseases. However, there are some areas in which the exact mechanisms remain unclear.

Differences in mechanisms could be due to the fact that PM with different origins have different chemical compositions that can activate via multiple pathways. Therefore, when investigating the cardiovascular effects of PM *in vivo* or interpreting the results, the role of different PM compositions must be taken into accounts.

Most of the studies used exposure methods other than inhalation, for example, intratracheal and intranasal instillation. Although these methods are reliable techniques for lung exposure, inhalation-based techniques provide a better simulation for airborne PM studies, given that the physical form and chemical composition of PM is preserved during inhalation.

Limited research has been carried out to explore the effects of urban PM from other origins such as dust.

To conclude, future studies should be conducted from the point of view of air pollution science. Mechanisms underlying the findings of related epidemiological studies remain uncertain and await clarification.

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***Source:*** Chemosphere, Vol. 242, Article 125204, March 2020.

# Mechanisms Underlying Disruptive Effects of Pesticides on the Thyroid Function

Thyroid hormones (THs; i.e. triiodothyronine [T3] and thyroxine [T4]) exert critical regulatory roles in cellular homeostasis. They control a number of physiological processes, including organ development, cell differentiation, cell growth and maintenance, and metabolism (i.e. anabolism and catabolism of carbohydrates, proteins, lipids, and damaged organelles).

The regulation of THs production and physiological action is complex and can be adversely disrupted through various intricate mechanisms by a broad spectrum of chemicals at environmentally relevant concentrations.

This study reviews the current knowledge on how some chemicals, especially pesticides, can disrupt TH homeostasis.

These disruptions include a) inhibition of TH biosynthesis in the thyroid follicular cells resulting in perturbation of the hypothalamic–pituitary–thyroid (HPT) axis; b) interference with TH transport proteins in the bloodstream; c) liver enzyme induction leading to increased inactivation and further excretion of TH from the body; d) interference with conversion of TH into the active form in peripheral tissues; e) interference with the transport of TH through cell membranes; and f) binding to intracellular TH receptors and further dysregulation of downstream gene expression sensitive to TH.

In the cumulative assessment group most pesticides named as contributors to "hypothyroidism" by the European Food Safety Authority (EFSA) affect the HPT axis through upregulation of TH elimination pathways.

Interspecies differences prevent extrapolation of some effects to humans. However, it has been noted that rats are markedly more sensitive than dogs and humans to TH perturbations. This difference in sensitivity largely relies on the difference in TH binding profiles and metabolic clearance rate of TH, which is considerably shorter in the rat.

Although the complex underlying processes have been relatively well characterized, a better understanding of the molecular mechanism behind the adverse effects of pesticides or at least their mode of action, would reduce the uncertainty when the combined risk of dietary exposure to pesticides is assessed according to the dose-addition model.

To this end, the cumulative assessment and common mechanistic approaches used by EFSA and the United States Environmental Protection Agency (US-EPA), respectively, benefit from expanded toxicological information on chemical structure, apical end points, and mammalian pesticidal modes of action. This will contribute to establishing key events in an adverse outcome pathway and will facilitate the movement toward a mechanistic-based risk assessment.

***Source:*** Current Opinion in Toxicology, Vol. 19, Pages 34-41, February 2020.

# Pesticides in the Urban Environment: A Potential Threat that Knocks at the Door

According to a joint report from WHO and UNEP, roughly 200,000 people in the world die, and around three million are poisoned each year by pesticides. The vast majority (95%) of cases occur in developing nations.

Pesticides play a pivotal role in controlling pests and disease, not only in urban agriculture but also in non-agricultural settings. Several pesticides are often applied at unintentionally or unneccesarity high concentrations, even in small urban areas such as lawns, gardens and impermeable surfaces.

Due to such inadvisable use in urban areas, both extensively and intensively, pesticide contamination now poses a serious threat to the environment, to living organisms and to food safety.

Pesticide residues often end up in waterways via stormwater runoff and contaminate both surface and groundwater. These contaminants are moved along in soil or plants and are spread throughout the environment by biotic and abiotic factors.

On a regular basis, many children and pets playing on lawns at home, in school and in public parks are readily exposed to pesticides or their residues. These poisons enter the human body through dermal contact, eye exposure, inhalation or ingestion. Homeowners consuming fresh fruits and vegetables obtained from household gardens often ingest pesticide residues as well.

The increased toxicity of urban pesticides, compared to agricultural pesticides, is a growing threat to the health and well-being of humans. Because soils, dust, air, water and food are likely to get heavily contaminated, urban pesticide use must be viewed with caution.

In fact, the fate and behaviour of pesticide residues in the urban environment are distinct from impacts in other ecosystems because the soils in urban areas vary so much in their physico-chemical properties. Development of sustainable and eco-friendly approaches for recovering urban soils contaminated with pesticides is therefore greatly warranted.

Further research in this area is needed for remediation of pesticide-contaminated urban environments to safeguard human health.

Suitable formulations of newer pesticides could be developed for their specific use in urban areas since most of the currently registered pesticides are potentially toxic to the nontarget biota.

The present critical review is the first inclusive source to provide updated knowledge on the sources, nature and extent of pesticide pollution in the urban environment, and the ecological and health effects on humans of pesticides and their residues.

***Source:*** Science of The Total Environment, Vol. 711, Article 134612, April 2020.

# WHO and IARC launches new Cancer Reports on 20th Anniversary of World Cancer Day

***On February 4th, 2020, the 20th anniversary of World Cancer Day, in response to government calls for more research into the scope of potential policies and programs to better control cancer, the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC), released two coordinated reports.***


Aimed at setting a global agenda, ***the WHO Report on Cancer: Setting priorities***, investing wisely and providing care for all is a call to stakeholders to mobilize and invest in universal health coverage. In view of the present and future global cancer burden, the report urges governments and health care providers to act now by applying the best current principles and tools for control and intervention.

If current trends continue unchecked, the world will see a 60% increase in cancer cases over the next two decades. The greatest increase in new cases (an estimated 81%) will occur in low- and middle-income countries, where survival rates are currently lowest.

The WHO document spells out the need to step up cancer treatment services in these countries. At least 7 million lives could be saved over the next decade by identifying the most appropriate science for each country situation.

Countries at most risk are now focusing their limited health resources on combating infectious disease and improving maternal and child health. However, these basic health services are ill-equipped to prevent, diagnose and treat cancer.

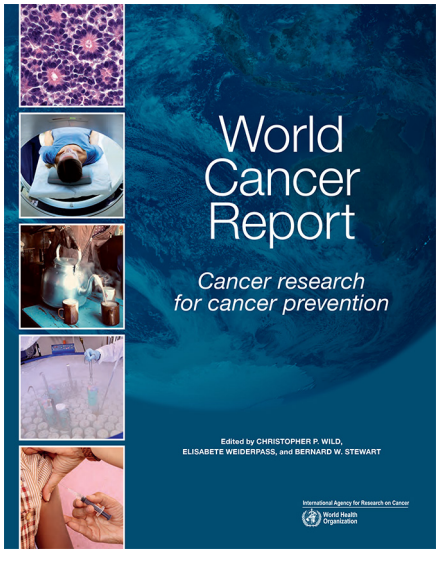
In 2019, more than 90% of high-income countries reported comprehensive treatment for cancer available in their public health system. In low-income countries, by contrast, the figure was less than 15%.

Cancer should not automatically be a death sentence for anyone, anywhere. With access to primary care and referral systems, more cases can be detected early, treated effectively, and cured.

The WHO report highlights a wide range of proven interventions to prevent cancer, especially, for example, controls on the sale and use of tobacco. Smoking is responsible for 25% of cancer deaths. Other basic strategies include screening and treatment, vaccinating against hepatitis B to prevent liver cancer, and eliminating cervical cancer by vaccinating against human papillomavirus (HPV). High-impact cancer management interventions bring value for money and should ensure access to palliative care, including pain relief.

***The World Cancer Report: Cancer Research for Cancer Prevention, published by the International Agency for Research on Cancer (IARC)***, was released in tandem with the WHO report.

Focusing on prevention, it offers the most comprehensive overview of relevant research available to date, ranging through studies in descriptive etiology, cellular and molecular biology, toxicology and pathology, and relevant advances in the behavioral and social sciences. Key chapters include discussions on the impact of a variety of inequalities associated with cancer, including vaccination and screening. Cancer prevention should improve, as well, when individual genomic




susceptibility to cancer is better understood and when those at risk can be more precisely identified.

The past 50 years have seen tremendous advances in cancer research and fewer deaths as a result, with greater focus on prevention, screening, early diagnosis and treatment. Between 2000 and 2015, wealthier nations implemented these strategies, providing better treatment for their citizens and achieving an estimated 20% reduction in the probability of premature mortality due to cancer. In the same period, by contrast, low-income countries saw only a 15% reduction.

Many countries are being challenged to balance considerations of cost, feasibility and effectiveness for their citizens suffering from cancer. There are cancer treatments, both innovative and established, which are effective and affordable, and which can provide benefits without causing financial hardship. Each government is tasked with choosing the appropriate therapies.

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***Source:*** WHO News Release and IARC News, 4 February 2020.

# Gestational and Perinatal Exposure to Diazinon Causes Long-lasting Neurobehavioral Consequences in the Rat

Diazinon is a widely-used organophosphate (OP) insecticide with substantial potential for environmental contamination and adverse effects on human health.

The efficacy of OPs in pest control has been principally linked to inhibition of the enzyme acetylcholinesterase, a mechanism that is well preserved in off-target species, including vertebrates like rodents and humans.

Epidemiological studies of populations with insecticide exposures suggest that early life exposure to organophosphates may have long-term effects on the brain and enhance the risk for psychiatric and neurodevelopmental issues later in life.

In human populations, it can be difficult to determine which specific compounds or risk factors are responsible for these effects, particularly later in life, so work with animal models has been conducted to evaluate the potential risk that specific compounds, like diazinon, may pose to the developing nervous system.

Studies with animal models, particularly rodents, have shown that pulsatile exposure to diazinon during neonatal development causes long-term neurobehavioral impairments in rats. However, the effects of chronic low concentration exposures during perinatal development remain unclear.

Based on the previous findings, it is hypothesized that, while diazinon exposures in gestational and perinatal development could produce persistent neurobehavioral effects, similar to neonatal exposures, but that the nature of those effects may be quite distinct.

The present study was conducted in Sprague-Dawley rats to evaluate developmental and behavioral endpoints in offspring with chronic low concentration exposures to diazinon across gestational and perinatal development.

The low level exposures were designed to fall below the threshold for overt toxicity in the dams or pups, and to approach the threshold for cholinesterase inhibition.

The gestational exposures were timed to overlap the first and second trimesters of human development during which key neurodevelopmental events take place. The lactational/neonatal exposures in the rat overlapped key neurodevelopmental events which take place in the human third trimester.

Offspring were monitored for neonatal health and growth, then assessed in a behavioral battery containing tests of locomotor, affective and cognitive functions from adolescence into early adulthood.

Chronic diazinon exposure from pre-mating until the neonatal period caused a significant increase in the percent of time spent on the open arms of the elevated plus maze, an index of risk-taking behavior.

Gestational and lactational diazinon exposure also caused a significant degree of hyperactivity in the figure-8 apparatus during adolescence, specifically affecting the early part of the hour-long test session. However, this effect dissipated by the time the rats reached adulthood.

Diazinon exposure also caused significant impairment in novel object recognition, a test of cognitive function. Compared to controls, offspring exposed to 228 μg/day diazinon showed significantly less preference for novel vs. familiar objects during the first five minutes of the novel object recognition test.

In summary, the present study detected multiple persistent consequences of low level perinatal diazinon exposure in behavior later in life with minimal cholinesterase inhibition.

These behavioral changes, which consisted of disruptions in open area avoidance in the elevated plus maze, brief hyperactivity in the figure-8 maze and impaired object recognition, spanned affective, locomotor and cognitive functions.

The brief hyperactivity effect was most apparent in the offspring of dams with lower level diazinon exposure and was most apparent among female offspring.

These varied behavioral changes corresponded with underlying effects on key neurotransmitter systems and included deficits in presynaptic acetylcholine activity, reductions in nicotinic acetylcholine receptors and reductions in serotonergic 5HT1A receptors. These effects were more pronounced in cortical and hippocampal tissues than other brain regions and were more pronounced in females than males.

The neurobehavioral consequences of gestational and perinatal diazinon exposure complement, but remain distinct from, the consequences of specific exposures during the third-trimester equivalent of human brain development, modeled through neonatal exposures in rodents.

These data underscore the potential risk posed by organophosphate insecticides like diazinon on the developing nervous system and further highlight the need for new and effective methods to identify and treat long-term effects on neurotoxic organophosphate exposures.

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***Source:*** Toxicology, Vol. 429, Article 152327, January 2020.




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