



# ABSTRACTS

## Conference Proceedings

All sessions presented at the  
7th International Conference  
on Children's Health and Environment

20-22 November 2013

Dan Panorama Hotel, Jerusalem, Israel

## *A Healthier World for Our Children*

Presented by

**INCHES**

**(International Network on Children's Health and Safety)**

(IN ALPHABETICAL ORDER  
BY FIRST AUTHOR'S LAST NAME,  
PRECEDED BY AN INTRODUCTORY PAPER  
CO-AUTHORED BY YONA AMITAI AND PETER VAN DEN HAZEL)

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## Children's Environment and Health—An Urgent Topic

Yona Amitai and Peter van den Hazel

Children are not little adults. They are human beings at a unique stage of life: a time during which they are the most vulnerable to their environments.<sup>1</sup> Because of a child's constant state of growth and development, she needs to be protected from soil, air, and water polluted by poisonous chemicals, heavy metals and harmful gas. These substances can affect the development and function of multiple biological systems, including the reproductive, endocrine, respiratory, neurological, and immune systems. According to the World Health Organization (WHO), poor environmental quality is responsible for 25% of all preventable illnesses in the world today. For children, this climbs to as much as two-thirds.<sup>2</sup> Unfortunately, threats from the environment are only made worse by unsustainable development, poverty, war, malnutrition, disease and neglect.

As a global community, we have reached a point in history where leaders at the highest levels are aware of the special susceptibilities of children and have shown initiative by publicly declaring that action is needed. Important partnerships were announced at the World Summit on Sustainable Development to facilitate this movement.<sup>3</sup> The European Union has put children's environmental health as one of the top priorities in its Strategy on Health and Environment, and health and environment is also a priority in the European Commission's Sustainable Development Strategy.<sup>4,5</sup>

The 7th International Conference on Children's Environmental Health and environment takes place in November 2013 in Jerusalem, Israel. The conference's scientific program, led by Dr. Ruth Etzel, professor of epidemiology at the University of Wisconsin, includes lectures, short oral presentations and posters presented by scientists from 16 countries covering a broad spectrum of topics. Abstracts of these presentations appear in the *Journal of Health & Pollution*.

In keeping with the overall aim of the conference, topics are related to: health effects of pollutants in children; prenatal exposures; reproductive health; cancer; obesity; biomonitoring; children's environmental health centers and specialty units; children's environmental rights; sustainable development; safety and injury prevention; and health policy.

The 7th INCHEM Conference will be concluded with the Jerusalem Declaration on Children's Environmental Health outlining future directions, goals and targets.

### Children's Environmental Health Issues in Israel

Israel is a nation with a youthful population and high fertility rate densely packed in a small geographic area, experiencing fast-paced economic and technological growth, intensive agricultural practices and scarce water resources. The underdeveloped transit system results in the high utilization rates of private motor vehicles. The crowded environment and proximity to pollution from transportation, industry and agriculture create environmental stresses that have particular impact on children's health.

Agriculture in Israel is a highly developed industry: Israel is a major exporter of fresh produce grown with



innovative agricultural technologies. While agricultural workers make up only 3.7% of the workforce, Israel produces 95% of its own food requirements. This type of intensive farming comes at a cost: a high use of pesticides. Recently, the Israeli Ministry of Environmental Protection and the Ministry of Health banned organophosphates and other pesticides, but pesticide exposure is still a major environmental problem. While public and media awareness of children's environmental health issues is increasing in Israel, there are still gaps in the teaching of these issues in medical schools and other health sectors, and in encouraging career development of professionals in the environmental health field.

The Environment and Health Fund (EHF), an NGO established in 2007, attempts to address some of the unique environmental health challenges in Israel. EHF funded the first comprehensive biomonitoring study in Israel, which revealed extremely high levels of organophosphate pesticide metabolites among Israelis. In addition, EHF established a Center of Excellence in Exposure Science at the Technion - Israel Institute of Technology in Haifa, which is at the forefront of national research on exposure to traffic-related pollution and related health endpoints. EHF has established a second center at the Hebrew University in Jerusalem, creating collaboration between the agriculture faculty and the School of Public Health to better understand the relationship between agricultural practices and human health. This center is a leader in research on the use of treated wastewater on edible crops. EHF has also funded a consortium of Israeli birth cohorts that is currently collecting and storing biological samples for future research on prenatal and early life exposures to environmental contaminants.

### **A Short History of INCHESES**

The International Network on Children's Health, Environment and Safety (INCHESES) was founded in August 1998 at a workshop meeting before the 1st International Conference on Children's Environmental Health in Amsterdam, the Netherlands, with the following goals:

- 1) To increase understanding of and accord on how environmental factors influence the health of children;
- 2) Globally disseminate research and information on children's environmental health;
- 3) Educate and facilitate information exchange on the best practices and policies in children's environmental health;
- 4) Identify information gaps and stimulate new research; and
- 5) Advocate for children's environmental health in the intergovernmental arena.

Since its founding, INCHESES has created an international network of 150 organizational members, including EURO-INCHESES and chapters in Russia, Germany and Italy; there are more than 30,000 individual members, mostly health professionals. Among its many achievements, the group has training programs in cooperation with several international universities, initiated several projects funded by the European Union, and organized conferences on children's environmental health.

### **The objectives of this year's conference is to:**

- Provide an international forum for the latest research findings in children's environmental health;
- Define the relationship between environmental contaminants and children's health;
- Strengthen the importance of prenatal exposure to environmental factors on pregnancy outcome and children's health;



- Identify opportunities to minimize childhood prenatal and postnatal exposure to environmental contaminants;
- Provide insight in the field of science and policy interface;
- Build a platform of knowledge at an international level;
- Develop a greater awareness among health professionals about children's health, environment and safety; and
- Initiate future directions and international collaborations in research in the field of children's environmental health.

This year's conference is organized by Bar Ilan University, Ramat Gan in collaboration with the Israeli Ministry of Environmental Protection, the Ministry of Health and international organizations; the Italian National Observatory on the Health of Children and Adolescence (PAIDOSS), the U.S. Environmental Protection Agency (EPA) and the European Environmental Agency (EEA). Sponsorship is provided by the Bar Ilan University, Neviot, and the Israeli government.

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## Air Pollution and Congenital Heart Defects

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**Background:** Environmental factors such as ambient air pollution have been associated with congenital heart defects (CHD). The aim of this study was to investigate the association between gestational exposure to air pollution and the risk of CHD.

**Methods:** We conducted a registry-based cohort study with a total of 135,527 live- and stillbirths in the Tel-Aviv region from 2000 to 2006. We used a geographic information system-based spatiotemporal approach with weekly inverse distance weighting modeling to evaluate associations between gestational exposure to ambient air pollution during weeks 3 to 8 of pregnancy and the risk for CHD. The following pollutants were studied: carbon monoxide, nitrogen dioxide, ozone, sulfur dioxide and particulate matter with aerodynamic diameter smaller than  $10\mu\text{m}$  and  $2.5\mu\text{m}$  (PM10 and PM2.5, respectively). Logistic models, adjusted for socio-demographic covariates, were used to evaluate the associations.

**Results:** Maternal exposure to increased concentrations of PM10 was associated with multiple CHD (adjusted OR 1.05, 95% CI: 1.01 to 1.10 for  $10\mu\text{g}/\text{m}^3$  increments). An inverse association was observed between concentrations of PM2.5 and isolated patent ductus arteriosus (adjusted OR 0.78, 95% CI: 0.68 to 0.91 for  $5\text{mg}/\text{m}^3$  increment). Sensitivity analyses showed that results were consistent.

**Conclusions:** Generally, there were no evidence for associations between gaseous air pollutants and CHD. Our results for PM10 and CHD confirm results from previous studies. The results for PM2.5 need further investigations.



## Ambient Temperature and Congenital Heart Defects

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**Background:** From rodents to non-human primates, teratogenic effect of hyperthermic insult has been demonstrated. There is less knowledge regarding the effect on the human fetus and ambient temperature. The aim of this study was to investigate whether maternal exposure during pregnancy to higher ambient temperature increases the risk of congenital heart defects (CHD).

**Methods:** This population registry-based cohort study included 135,527 live- and stillbirths in the Tel-Aviv region from 2000 to 2006. Two clinical diagnostic groups of isolated cardiac defects and a group of multiple cardiac defects were studied. Temperature measurements were constructed from ambient stations. Maternal exposure to average ambient temperature and extreme heat events (daily average temperature above the 90th percentile) during weeks 3 to 8 of pregnancy was assessed. Logistic models, adjusted for socio-demographic covariates were used to evaluate the associations between temperature and CHD risk.

**Results:** In general, we did not find significant associations between ambient temperature and CHD throughout the year, with an exception for multiple CHD. After stratifying by season of conception, it was found that, during the cold season, continuous exposure to average ambient temperature and maximum peak temperature (1°C increase) increased the risk for multiple CHD (OR 1.05, 95% CI: 1.00, 1.10 and OR 1.03, 95% CI: 1.01, 1.05, respectively). A 1-day increase of extreme heat events increased risk for multiple CHD (OR 1.13 95% CI: 1.06, 1.21) and also for isolated atrial septal defects (OR 1.10 95% CI: 1.02, 1.19).

**Conclusions:** Increased risk for CHD in association with elevated temperature may be important in the light of climate change and global warming.



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## The Expanding Role of PEHSUs in Public Health

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**Background:** Pediatric environmental health specialty units (PEHSUs) originated 15 years ago in the United States to better manage the health consequences of toxic environmental exposures to infants, children, and young adults.

**Methods:** PEHSUs combine the professional expertise of several essential medical disciplines – pediatrics, occupational medicine, environmental toxicology, and others.

**Results:** PEHSUs provide a specialized referral resource for clinicians as well as risk assessors, environmental scientists, project managers, and others responsible for environmental protection and cleanups. However, PEHSUs also play an important role in public health – expanding public education, training primary care physicians and other health professionals, and consulting for various environmental problems and emergencies.

**Conclusions:** This session features several prominent individuals whose experiences with PEHSUs provide cogent examples of the types of support communities and health professionals receive from these invaluable public health assets.

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## Lessons From Children's Environmental Health: Vulnerabilities in Community-Wide Emergencies

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**Background:** Community-wide emergencies sometimes display patterns that resemble the aftermath of chemical spills and other types of environmental exposures. Whether a chemical release results from a



truck accident or a terrorist attack, the cascade of events that follow can be nearly identical.

**Methods:** Standardized approaches— identification, risk assessment, containment, remediation, recovery—are vital in both scenarios. In particular, both scenarios most commonly involve populations with infants and children.

**Results:** Pediatric environmental health specialty units (PEHSUs) can be extremely valuable to public health authorities and emergency planners seeking to develop community response plans that incorporate the heightened vulnerabilities and requirements of this special population. PEHSU professional staff and other child advocates are critical players in community-wide emergency planning, and must insist that measures to handle putatively exposed children are tightly woven into master plans and not simply deferred to future revisions.

**Conclusions:** It is axiomatic that, in most instances, good risk management for the most vulnerable also protects the general population. Conversely, a public emergency plan that does not plan for children is not an adequate plan.

## Toward a European Environmental Health Narrative: Storybooks For, By and With Children

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**Background:** In connection with ongoing work by the European Environment Agency’s Network of National Reference Centers on Environment and Health, a European environment and health narrative is being prepared. This work and narrative will draw upon experience from long-time activities in the EU on children’s environmental health, notably based on the EU’s environment and health strategy, SCALE (Science-Children-Awareness-Legal-Evaluation).

**Methods:** Children constitute a special part of the human population in many ways, not just through their particular vulnerability to health-impairing agents; these characteristics will be more thoroughly evaluated for an influential ‘sub-narrative.’ Children, in essence, constitute a prism through which environmental health can be focused and organized, both in terms of reflection and communication and action. Children also call for and enable new approaches to analyzing and communicating about environmental health, such as uniting cognitive/evidential with emotional/experiential aspects, and local/familial with EU-wide/global aspects.



**Results:** The health-promoting qualities of green and varied environments are of particular importance for children's health, including the importance of exercise and the outdoors for healthy life and learning. Such influences underline the need to extend environmental health studies and assessments from health-impairing agents to spatial planning and social rejuvenation, and to reach out to audiences in new ways.

**Conclusions:** Children as a particular population segment are crucial in their own right but also useful more generally in developing effective environmental health narratives, providing both challenges and opportunities.

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## War and Children's Environmental Health: Continuity and Change in the 20th Century

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**Background:** Wars constitute crucial factors in children's environmental and general health and safety, but are under-represented in studies, assessments and discourses.

**Methods:** Wars and armed conflicts in children's environmental health during the 20th century are explored, focusing on northeastern Europe, especially Finland and the Baltic states, to identify underlying factors of change and continuity, and opportunities for prevention and care. Sample analyses of documents and recollections of those engaged in wars and conflicts are employed to complement conceptual analysis of drivers, processes, outcomes and interventions, in a structural-phenomenological discourse analytical approach. Health risk and impact assessment paradigms are extended to include social and mental health beyond biomedical aspects, exposures to stressors and trauma beyond immediate effects of warfare, and dynamics in processes.

**Results:** Wars and their health impacts and prevention/care are framed broadly, encompassing adjacent processes (e.g. migrations/deportations, ethnic/group violence), stressors and their impact (famines and other constraints on basic resources; epidemics; natural/semi-natural disasters; disrupted family ties and social fabric). The conceptual analysis traces connections and contingencies between structural factors and phenomena, specifying types of conflicts and exploring differences and commonalities in processes of aggression against those considered outsiders. Attention is paid to the sensitivities (vulnerabilities and capabilities) of children, and to the significance of personal and inter-generational working memories as keys to care and prevention.



**Conclusions:** Wars influence children's environment, health and safety in profound, yet poorly known ways that can be better delineated using multi-method approaches.

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## Governing Health Risks from Contaminated Artificial Groundwater: Multi-Perspective Approach for Defining Acceptable Risk and Uncertainty

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**Background:** In both water-scarce and water-rich regions, potable water is threatened by chemical and biological contamination of natural water reserves. This is also true of water-recycling systems such as groundwater aquifers recharged with surface water.

**Methods:** Conceptual models for assessing and evaluating health risks in the context of monitoring and managing an aquifer recharged by river water in southwest Finland were developed by a three-fold methodology: 1) establishment of frameworks for action-oriented health risk assessment including exposure, effects, and risk-benefit analyses; 2) assessment of public concern based on expressed opinions of professional and lay people in media; and 3) expert-generated meta-models of risk scenarios incorporating intervention point analyses. The framing, characterization and heuristics for decisions were specified. The methodology was tentatively applied to children's health risks, in partial differentiation approach, as a framework for closer evaluation based on empirical data.

**Results:** Framing of risk and distribution of exposure, risk and impact (including benefits from potable water, compared with baseline options) in time, regionally and among groups of children essentially influence management decisions, e.g. with sudden peaks of risks. Needs for measurement data and risk reduction options are evaluated.

**Conclusions:** Multi-perspective, reflexive methods capturing different notions of risk, uncertainty and their significance for children's health are both needed and feasible.



## Indoor Air Quality of Urban Hookah Bars

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**Background:** Despite declines in cigarette use in the U.S., the use of alternative tobacco products, such as hookahs, is increasing dramatically among adolescents. This is largely due to a paucity of knowledge about the deleterious effects of mainstream and second-hand hookah smoke. No study to date has characterized levels of particulate matter (PM), a strong indicator of pollution from tobacco smoke, and black carbon (BC), a respiratory tract irritant and possible carcinogen, in urban hookah bars.

**Method:** Measurements of PM and BC levels in 2 hookah bars in New York city were obtained by personal data rams and aethalometers. The data rams recorded the total PM concentrations (PM<sub>10</sub>; PM<sub>2.5</sub>), and the aethalometers recorded BC levels (total and PM<sub>2.5</sub>) in real time. Samples are also collected on Teflon and quartz filters for gravimetry, trace elements/metals and organic/elemental carbon analysis.

**Results:** We found that the PM concentrations reached approximately 250 µg/m<sup>3</sup> (The U.S. Environmental Protection Agency categorizes 201-300 as “very unhealthy”). BC concentrations varied between 6-8 µg/m<sup>3</sup>, with some readings as high as 19 µg/m<sup>3</sup> over an hour in urban hookah bars (major U.S. cities generally have background levels from 0.3-2.5 µg/m<sup>3</sup>).

**Conclusions:** This is the first study to demonstrate that air pollutants in hookah bars far exceed EPA standards and U.S. city norms for PM and BC that are likely to result in adverse pulmonary and cardiovascular effects. These findings may have profound implications on an emerging public health threat, while providing key information relevant to tobacco control policies and regulations.



## Identifying Life Stages for Monitoring and Assessing Risks From Environmental Contaminant Exposure: A World Health Organization Review

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**Background:** A more scientific basis is needed for identifying vulnerable life stages for various environmental exposure scenarios. Currently, available approaches have limited applicability due to the range of geographic, social, cultural and economic diversity in populations worldwide.

**Methods:** The World Health Organization convened a group of experts to provide guidance on critical life stages for use in exposure and risk assessment. The objective was to propose a fit-for-purpose set of life stages. Exposure-related issues to consider in determining the most appropriate age ranges and life stages for risk assessment were summarized.

**Results:** A harmonized set of age bins for monitoring and assessing risks from exposures to chemicals was proposed for global use. The focus is on pre-conception through adolescence, though the approach is applicable to additional life stages. A 2-tiered set of early life age groups is recommended. The first tier involves adoption of guidance similar to the childhood age groups recommended by the U.S. Environmental Protection Agency (EPA); the second tier consolidates some of those age groups to reduce burden of developing age-specific exposure factors for different regions.

**Conclusions:** While there is no single “correct” means of choosing a common set of age groups to use internationally, a common set of age groups is recommended to facilitate comparisons of potential exposures and risks around the globe, collection of data, and analyses of aggregate exposure and cumulative risk. Application of these age groups for robust assessment of exposure and risk for specific populations will require region-specific exposure factors as well as local environmental monitoring data.



## Exposure to Chlordecone and Thyroid Hormone Levels in 3-Month-Old Infants

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**Background:** The insecticide chlordecone was extensively used in the French West Indies to control *Cosmopolites sordidus*. Its persistence in soil has led to the widespread pollution of the environment, and human beings are still exposed to this chemical. Chlordecone, a recognized endocrine disrupter, has been shown to impair neurological and behavioral functions in rodents when exposure occurs during gestation or as neonates. The aim of the study was to evaluate the association between prenatal and postnatal exposure to chlordecone and neonatal levels of thyroid hormones in 3-month-old infants (n=111) from Guadeloupe.

**Methods:** Samples of cord blood (n=111) and breast milk at 3 months (n=92) were analyzed for chlordecone, PCB153 and pp'-DDE concentrations. Postnatal exposure was determined through breastfeeding. Levels of thyroid-stimulating hormone (TSH), free triiodothyronine (fT3) and free thyroxine (fT4) were measured in the infants' blood at 3 months.

**Results:** Cord chlordecone concentration was associated with increasing levels of TSH after adjustment for covariates and co-exposures, especially among boys. No association was observed with fT3, fT4 levels or with postnatal exposure to chlordecone through breastfeeding.

**Conclusion:** Although based on small numbers, these results suggest that prenatal low chronic exposure to chlordecone is associated with TSH levels at 3 months. These modifications will be interpreted in the light of observations of impairments in fine motor function in boys aged 18-months evaluated in the same population.



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## Moving Towards Improved Prenatal Environmental Health Education in Canada

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**Background:** There is growing recognition that low-level exposures to toxicants in our day-to-day environments negatively impact the health of the fetus and young children. The prenatal period is the most vulnerable time as exposures can interfere with healthy growth and lead to developmental defects that may have lifelong consequences. In the Canadian context, little is known about the extent to which prospective parents are aware of prenatal environmental health issues or about the sources and nature of any education they may be receiving.

**Methods:** A telephone survey (n=606) and qualitative interviews (n=14) were conducted with new mothers in Ontario, Canada. Topics explored included: environmental risk awareness and perceptions; sources of information; and protective action. This was combined with a scan of Canadian and international educational programs and resources related to prenatal environmental health.

**Results:** From the survey, we found a low level of concern and limited awareness with only 55% of new mothers reporting to have received any information about environmental health risks to their children since getting pregnant. Of those who received information, only 11% reported that it came from a prenatal health care provider. In our scan, we identified numerous educational initiatives outside of the health care system. However, little is being done within the system.

**Conclusion:** While considerable information is available to prospective parents from web sites and other sources, relatively few appear to be seeking it out. A more systematic approach to prenatal environmental health education is required. This will be discussed in the context of an evolving prenatal environmental health education initiative being developed in Canada.



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## Developing a Regional Children's Environmental Health Center—Successes and Challenges

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**Background:** Children are the “canaries in the coal mine” when it comes to environmental issues. Children in the most crowded and resource-poor neighborhoods are at highest risk, exposed to greater environmental burden, and their families and communities are least equipped to mitigate such problems. The disease most closely linked with our environment is asthma, and the prevalence continues to rise. Practicing physicians receive limited training in environmental health and often do not have access to local expertise.

**Methods:** We present our efforts to develop a regional Children's Environmental Health Center as a unique collaboration of public health faculty and pediatric pulmonologists at the Maria Fareri Children's Hospital and New York Medical College. The mission includes clinical consultation, education, research, and advocacy. There are a number of unique characteristics of this center: (1) grounded in a large clinical program, with 9 outreach offices throughout a large geographical region which permits rapid dissemination of services to children and families; (2) suburban location, unlike most centers that are located in large cities with primary focus on urban environmental concerns; (3) staffed mostly by pediatric pulmonologists, a clinical subspecialty that has not frequently ventured into children's environmental health; (4) developed without significant extramural financial support, and needed to rapidly develop strategies to support our efforts in large part with clinical income.

**Results:** We present clinical vignettes and review our successes and challenges.

**Conclusions:** Developing a self-sustaining regional children's environmental health center is a challenging and rewarding process that can be duplicated world-wide.



## Congenital Malformations in Infants Conceived Following Assisted Reproductive Technology in Comparison with Spontaneously Conceived Infants

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**Background:** To evaluate the risk for congenital malformations diagnosed at birth following assisted reproductive technology (ART) treatments compared with live births conceived spontaneously.

**Methods:** A retrospective cohort study including 9,042 live births following ART and 213,288 spontaneously conceived (SC) live births during the period from 1997 to 2004. The cohort was linked to the national live birth registry to determine the outcome of the pregnancies, including congenital malformations.

**Results:** An increased adjusted risk for all congenital malformations was observed in infants born via ART treatments compared with spontaneously conceived infants [2.4% vs. 1.9%; OR adj.=1.45; 95% CI: 1.26,1.68]. The increased risk was observed in singleton births [2.4% vs. 1.8%; OR adj.=1.41; 95% CI: 1.14,1.71] but not in ART-conceived multiple births [2.5% vs. 2.6%; OR adj.=1.15; 95% CI: 0.90,1.46]. Significantly increased adjusted risks for nervous, circulatory, digestive and genital system malformations were evident in the ART singleton group compared to SC infants. In addition, increased risks were also observed in separate comparisons of in vitro fertilization births versus SC [OR adj.=1.28; 95% CI: 1.00,1.63] and intracytoplasmic sperm injection births versus SC [OR adj.=1.56; 95% CI: 1.31,1.84]. Data regarding pregnancy termination or congenital malformation diagnosed later in life were not included.

**Conclusion:** Infants born following ART were at significantly increased risk for congenital malformations compared to live SC births.



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## Treatment and Prevention of Childhood Lead Poisoning: New Approaches to Management Of Children with Long-Term Environmental Exposure

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**Background:** There are many regions in the world where large populations of children are still adversely affected by long-term industrial lead pollution. New strategies appear to be needed for both treatment and prevention of the childhood lead poisoning, particularly in situations in which traditional chelation therapy is not feasible. In situations where repeated chelation therapy seems unavoidable, we propose considering substitution of various synthetic chelating agents with a choice of natural substances which act as mild and safe chelators. Some products have already undergone pre-clinical research as well as clinical trials involving children. The substances are commonly classified as nutraceuticals, or dietary supplements, and are generally regarded as safe. A major advantage is that the use of these supplements does not necessitate the existence of a health care delivery system dedicated to the particular environmental health problem.

**Methods:** A review of potential new approaches for the treatment of childhood lead poisoning will be presented.

**Results:** We believe that one of the key processes in lead poisoning to be targeted is neuro-inflammation. Results from experimental studies hold promise that certain natural substances may actually provide a remedy or protection against lead-associated injury to the nervous system.

**Conclusions:** New knowledge about the mechanisms of lead toxicity at the biochemical level opens up possibilities for additional therapeutic and preventive modes of intervention beyond chelation therapy, including neuro-protection. Some natural substances may protect the child's developing nervous system.



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## Awareness-Raising on Hazardous Chemicals for Parents, Health Experts and Political Decision Makers: An Overview of Best Practices

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**Background:** Studies show that endocrine-disrupting chemicals (EDC) play a role in disrupting human brain development, deterioration of male reproductive health, increased incidence of male and female hormone-related cancer, and increase in cardiovascular disease, obesity and diabetes. Most vulnerable groups are pregnant women, neonates and children.

**Methods:** The Women in Europe for a Common Future's (WECF's) program Nesting is conducted in 10 countries and will soon expand to Latin America and Portugal. Activities include informational websites and publications, a mobile app, workshops, and training programs.

**Results:** There are approximately 7,000 visitors per month to the Nesting Internet portal, and about 200,000 informational brochures have been disseminated to parents, politicians, child care and health professionals. In Germany, there have been 7,000 mobile app downloads since August 2013, and 3,000 individuals have participated in environment and health workshops provided by WECF.

**Conclusions:** WECF aims to inform parents and the health sector about concrete measures to prevent exposure to EDCs and other harmful chemicals. Within several projects we work on different target groups to raise awareness, improve the legal situation and give concrete information to consumers.

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## Neonatal Exposure to Phthalates: Links to Obesity and Asthma

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**Background:** Rising levels of asthma and obesity in children and young adults is a problem of significant



public concern. Population-based studies indicate that exposure to environmental contaminants is associated with childhood asthma and obesity. In the present study we investigated the effects of neonatal exposure to phthalates on biochemical mechanisms important in both asthma and obesity. It is our thesis that early childhood exposure to phthalates and/or their metabolites results in alterations to specific metabolic pathways important in asthma and obesity in mesenchymal stem cells, including peroxisome proliferator protein expression and activity and the leptin-EGFR-Notch axis.

**Methods:** The purpose of this study was to characterize MEHP-induced changes in PPAR-g signaling in adult and neonatal neutrophils as well as mesenchymal stem cells. Neutrophils were treated with MEHP (250-500  $\mu$ M) or medium control, in the presence or absence of troglitazone (TgT), a PPAR-g agonist. Mesenchymal stem cells were treated with MEHP (10-500  $\mu$ M). Chemotaxis was measured using modified Boyden chambers, Annexin V binding, and H<sub>2</sub>O<sub>2</sub> production by Amplex Red fluorescence. Inflammatory cytokines were quantified by cytometric bead array analysis. Gene expression was measured by real-time PCR or PCR array.

**Results:** MEHP induced inflammatory activity in neutrophils, as indicated by increased chemotaxis and decreased apoptosis. These effects were markedly increased in neonatal cells, compared to adult cells. Similarly, MEHP induced H<sub>2</sub>O<sub>2</sub> production in neonatal, but not adult, neutrophils. MEHP increased IL-8 production 4-fold in neonatal neutrophils, while adult cells were not affected. IL-1b production was increased 6-fold in neonatal neutrophils compared to 2-fold in adults. The effects of MEHP on H<sub>2</sub>O<sub>2</sub> and IL-1b production were reversed by troglitazone.

**Conclusions:** MEHP-induced H<sub>2</sub>O<sub>2</sub> production and generation of inflammatory cytokines were increased in neonatal neutrophils, and this was associated with reduced apoptosis and chemotaxis. Thus, neonatal neutrophils were more susceptible to the pro-inflammatory and pro-oxidant effects of MEHP than adult cells. These responses were mediated, in part, by inhibition of the PPAR-g signaling pathway and may increase the susceptibility of neonates to inflammatory disease.

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## Predictors of Emerging Alternative Tobacco Products Use among Adolescents

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**Background:** While adolescent cigarette smoking is declining in the U.S., there is great public health concern about the increasing use of emerging alternative tobacco products (ATPs). Yet little is known about factors associated with ATP use.



**Methods:** Bivariate and multivariate analyses were conducted using data from the 2011 National Youth Tobacco Survey to explore factors associated with current use of 5 ATPs: hookahs, bidis (thin, hand-rolled cigarettes), kreteks (clove cigarettes), cigars/cigarillos, and dip. Characteristics studied included: age, sex, and ethnicity; cigarette use; ATP use by family members; weekly spending; ease of access; and peer pressure concerning cigarettes.

**Results:** The nature of the association varied widely by factor and particular ATP. For example, those  $\geq 17$  years, compared to those  $\leq 13$ , were more likely to use hookahs (1.6, 2.7-5.4) and cigars (1.5, 1.1-2.1), but were less likely to smoke bidis (0.2, 0.1-0.3) or kreteks (0.2, 0.1-0.4). Similarly, there were marked gender and racial/ethnic differences in use of each ATP. In contrast, use of a particular ATP by family members was the only factor positively associated with the use of each ATP, e.g. adolescents with a kretek user in the family were 18.1 times more likely (95% CI 6.2 - 52.4) to also smoke kreteks.

**Conclusions:** This is the first study to comprehensively examine predictors of ATP use in a nationally representative sample of U.S. adolescents reporting on their own use of 5 ATPs. It demonstrates unanticipated differences in characteristics associated with use of each ATP, which may have marked implications for addressing this public health threat.

## Monitoring Children's Health in Contaminated Sites

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**Background:** Despite the known susceptibility of children to ambient pollutants and some documented causal associations, the epidemiological literature addressing the health risks in children residing in contaminated areas is scarce. In Italy, SENTIERI KIDS is an ongoing project aimed at monitoring children health at national priority contaminated sites (NPCS). About 1 million children (<20 years) live in 44 NPCS, and among those aged between 0 and 1 year, preliminary data show an increased mortality risk from all causes and from perinatal conditions equal to 4% and 5%, respectively.

**Methods:** For each site, index pollutants will be identified based on toxicological properties and contamination levels. An a priori evaluation of the epidemiological evidence linking health outcomes to residing in NPCSS will be carried out; socio-economic information will be examined to define a specific deprivation index for children.

**Conclusions:** SENTIERI KIDS is the first project specifically aimed to assess the health profile of children living in contaminated areas through an innovative approach based on multi health outcomes (mortality, cancer incidence and hospital admission records).



## Content Validation of a Questionnaire Designed to Explore Pediatric Environmental Risk Factors

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**Background:** Evidence is growing that the environment plays a large role in various pediatric conditions. Questionnaires are the predominant tools assisting clinicians to assess environmental health. Without being tested for validity and reliability before application, they can lead to clinical error and biased interpretations. The Pediatric Environmental Health History (PEHH) questionnaire created by us is no exception and underwent content validation.

**Methods:** Environmental health experts were identified mainly through pediatric environmental health specialty units, in which their opinion on question relevancy of an online survey was required for 200 questions spanning 9 sections. A second version (249 questions) was then generated based on their suggestions and reiterated. Percent Agreement (PA), the average percent of experts rating an individual question as relevant per section, and Universal Agreement (UA), the percent of questions per section agreed upon by all experts, were determined as measures of content improvement.

**Results:** For the first round, involving 10 experts, PA and UA ranged 79%-94%, and 14%-64%, respectively, indicating good consensus on specific questions but low overall agreement due to highly subjective responses. The reiteration included only 8 of the original experts, in which the PA and UA changed to 62%-98% and 36%-85%, respectively. Eight sections had PAs above 90%, whereas only 1 section, General Environment (62%) required further improvement.

**Conclusion:** After 2 expert reiterations, the PEHH reached more response homogeneity and therefore content improvement. Current application of the questionnaire indicates satisfaction of parents/guardians; we are awaiting pediatrician comments.



## Maternal Social, Psychological and Nutritional Factors in Exclusive Breast-feeding and Child Neuropsychological Development: A Cohort Study

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**Background:** The study investigates whether the duration of exclusive breastfeeding is associated with child neuropsychological development and whether this association is explained by social, psychological and nutritional factors.

**Methods:** This is a birth cohort study undertaken in the city of Sabadell (Catalonia, Spain). Women were recruited between 2004–2006, during the first trimester of pregnancy. Information about parental characteristics and breast-feeding was obtained through questionnaires. Exclusive breast-feeding was categorized as never; short-term ( $\leq 4$  months); long-term (4–6 years); and very long-term ( $> 6$  years). A trained psychologist assessed neuropsychological development at 4 years of age using the McCarthy Scales of Children's Abilities ( $n = 434$ ).

**Results:** Exclusive breast-feeding showed an independent association with child general cognitive score after adjusting for a range of social, psychological and nutritional factors ( $> 6$  months, coef. [95% CI]: 7.4 [2.8 to 12.0],  $p$ -for-trend = 0.011). Maternal social class, education level and intelligence quotient were also associated with child general cognitive scores, but did not explain breast-feeding associations. N3-fatty acid levels were not associated with child general cognitive scores.

**Conclusions:** Very long-term exclusive breastfeeding was independently associated with 4-year-old neuropsychological functions. Maternal indicators of intelligence, psychopathology and colostrum n3-fatty acids did not explain this association.



## Nutritional and Socio-demographic Cofactors of Prenatal Methylmercury Exposure and Genetic Predisposition to Cognitive Deficits

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**Background:** Assessment of cognitive consequences associated with prenatal methylmercury exposure in school-aged children may need to take into account nutritional and socio-demographic cofactors, as well as relevant genetic polymorphisms.

**Methods:** Mercury concentrations were measured in freeze-dried umbilical cord tissue of a sub-sample of the Avon Longitudinal Study of Parents and Children (Bristol, UK) as a measure of methylmercury exposure. A total of 1,135 children had available data on 247 single nucleotide polymorphisms (SNPs) within relevant genes, as well as the Wechsler Intelligence Scale for Children Intelligence Quotient (IQ) scores at 8 years of age. Multivariate regression models were used to assess the associations between methylmercury exposure and IQ, and to determine possible gene-environment interactions.

**Results:** Mercury concentrations indicated low background exposures (mean = 26 ng/g, standard deviation = 13). Log<sub>10</sub>-transformed mercury was positively associated with IQ, which attenuated after adjustment for nutritional and socio-demographic cofactors. In stratified analyses, a reverse association was found in higher social class families (p-value for interaction = 0.0013, performance IQ), among whom there was a wider range of methylmercury exposure. Among 40 SNPs showing nominally significant main effects, methylmercury interactions were detected for rs662 (paraoxonase 1) and rs1042838 progesterone receptor) (p < 0.05) and for rs3811647 (transferrin) and rs2049046 (brain-derived neurotrophic factor) (p < 0.10).

**Conclusions:** In this population with low-level methylmercury exposure, there were only equivocal associations between methylmercury exposure and adverse neuropsychological outcomes. Heterogeneities in several relevant genes suggest possible genetic predisposition to methylmercury neurotoxicity in a greater proportion of the population. Future studies are needed to address this possibility.



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## Changes in the Anthropometric Parameters Of Ukrainian Newborns Across Multiple Generations

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**Background:** Changes in the parameters of the physical development of a population reflect changes in the gene pool. These differences can be used as indicators of a population's adaptation to environmental shifts. The purpose of this study was to identify developments in the anthropometric parameters of Ukrainian newborns across multiple generations.

**Methods:** Neonatal weight and height data from residents of the cities of Cherkasy, Kiev and Zhytomyr were gathered from a group of studies done approximately 20 years apart, including periods before and after the 1986 Chernobyl nuclear disaster. The data was analyzed for changes in anthropometric parameters. The mean values of absolute and relative indices of physical development of infants were determined.

**Results:** There was a decrease in the general weight and height coefficient for children born in the 21st century, compared to previous generations. These changes were expressed more in boys than in girls, and, post-Chernobyl, were equally observed in contaminated and non-contaminated regions.

**Conclusion:** Negative changes were noted for polygenic parameters of weight and neonatal height in children born in the 21st century compared to previous generations. This could be regarded as the result of epigenetic influences. Changes testify to the possibility of reduced adaptive properties in the current generation, which may later evidence itself in the health of the general population. Determination of the mechanisms responsible for these outcomes requires further research.



## Exposure to Metals and Congenital Anomalies in Bedouin Women Living Near an Industrial Park: a Biomonitoring Pilot Study

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**Background:** Southern Israel's Bedouin population is, on average, of a low socio-economic status. Smoking among males and consanguineous marriages are frequent. Previous studies have shown elevated rates of major malformations within the Bedouin population residing near a large industrial park compared to other, more remote localities (5.6% vs 4.8%,  $p < 0.01$ ). Exposure to metals has been related to birth defects, and high ambient values of arsenic and nickel were detected based on reports. We estimate the extent of exposure to metals in pregnant Bedouin women to be in relation to birth outcome.

**Methods:** We enrolled 60 Bedouin women into our study upon their admission to deliver at a local hospital. Maternal urine samples were collected and maintained at  $-20^{\circ}\text{C}$  till tested for metals in the clinical toxicology lab at Sheba Medical Center, Tel HaShomer. A medical history on pregnancies, consanguineous marriages, and parental metal exposures was collected for each patient.

**Results:** Aluminum was detected in 5 out of 30 women (16.7%), arsenic in 6 out of 60 women (10.0%), and cadmium was under the level of detection level (1 mg/l), in spite of a high rate of smoking among Bedouin males, indicating low maternal passive-smoking exposure. This amounts to 10 women (16.7%) positive to any of the 3 metals. Three out of 10 fetuses exposed to metals (30%) had anomalies and 1 fetus died in utero, compared to 16.0% (8 out of 50) with anomalies within the unexposed group. Mothers living closer to the industrial park tended to have greater exposure to metals, give birth earlier and at a lower weight ( $p = 0.06$ ).

**Conclusions:** Our findings urge for further screening for metals in susceptible populations in Israel.



## Exposure to Phthalates: Results from the EU Twin Projects COPHES/DEMOCOPHES

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**Background:** Exposure to chemicals is quantified in Germany on a population-representative basis by the German Environmental Survey (GerES). The main aims of this and the EU-wide human biomonitoring (HBM) studies are the investigation of internal exposures to toxics and identification of major sources of exposure.

**Methods:** In the first harmonized EU-wide HBM twin studies COPHES/DEMOCOPHES, cadmium, cotinine, and phthalate metabolites in urine were analyzed in Germany and 16 other European countries. The HBM data gained from 120 German mother-child dyads were compared to GerES IV and European data with respect to age, and national representativeness.

**Results:** Exposure of mothers and children in the German DEMOCOPHES study differ to some extent from GerES results. Lower mean exposure levels for phthalates are in accordance with time trends observed in Germany and may be a result of exposure reduction measures. However, some DEMOCOPHES children exceed HMS value I indicating an exposure level above which adverse health effects cannot be ruled out completely. DEMOCOPHES results reveals higher exposure in children using personal care products or eating fast food more often.

**Conclusions:** COPHES/DEMOCOPHES is a first step to get information on the presence of environmental chemicals in Europe. These results give clues to sources and substances to be further investigated in GerES V to scientifically support policy making.



## Exposure of German Children and Young Adults to Chemicals of Concern: Using Human Biomonitoring to Prioritize New Investigations

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**Background:** Europeans are still exposed to a substantial amount of chemicals. While in the past, ambient air and drinking water were particularly significant sources of exposure, today's are food, indoor air, cosmetics, and consumer products. Toxicological and epidemiological studies have revealed associations between exposure and health effects for numerous substances. In Germany, exposure to various chemicals is well documented by the German Environmental Survey (GerES) and the Environmental Specimen Bank (ESB).

**Methods:** After identifying substances of toxicological relevance to which the general population might be exposed, new human biomonitoring (HBM) methods for the sensitizing agent methylene diphenyl diisocyanate (MDI), the plasticizers Hexamoll® DINCH® and di(2-propyl heptyl) phthalate (DPHP), and parabens have been developed and—if appropriate—applied to ESB samples.

**Results:** While MDI and DPHP seem not to be related with a measurable exposure of individuals not occupationally in contact with the substances, DINCH levels have been increasing constantly since its introduction. The relevance of these findings is to be assessed by derivation of toxicological human biomonitoring values as well as by HBM studies in the population-representative GerES V.

**Conclusions:** HBM helps to prioritize further toxicological investigations into a continuously changing chemical landscape and provides guidance on consumer decisions and policy. However, on-going monitoring of established toxic substances is essential for assessing impacts of chemicals on children.



## Community Lead Exposure of Children in Developing and Emerging Economies: Problems, Policies, and Solutions Based on Case Studies in Eastern Europe, Caucasus, and Central Asia

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**Background:** Throughout the former Soviet Union, the health of millions of children remains affected by environmental factors, including lead contamination. Although 75% of children in certain urban areas are at risk, childhood lead poisoning as an important public health problem in the region has not been recognized. There is also a lack of adequate surveillance and awareness of the problem among the international community.

**Methods:** The American Industrial Hygiene Association (AIHA), in collaboration with the International Task Force for Children's Environmental Health, has developed a reference document reviewing the lead exposure situation among children in the post-Soviet Union territories. It proposes potential solutions based upon a number of environmental and clinical investigations.

**Results:** In urban residential soil, lead concentrations up to 24,000 ppm (parts per million) have been measured. There is a high prevalence of elevated blood lead levels, with levels reaching 100 µg/dL in pre-school children. Hundreds of thousands children are estimated to be at risk for lead poisoning in the former Soviet Union. Remediation activities are unfortunately very few, if any. Discussion points to be presented include proposed recommendations on international safety standards to prevent childhood poisoning, evaluation of innovative approaches for interventions and treatment of children; new approaches and technologies for the early detection and monitoring of childhood lead poisoning, including modernized zinc protoporphyrin (ZPP) testing.

**Conclusions:** The international community should play a more active and significant role in the prevention of childhood lead poisoning in the former Soviet Union and other high-risk regions of the world.



## Obesity-Associated Sensorineural Hearing Loss in Adolescents

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**Background:** Childhood obesity is a profoundly important clinical and public health problem associated with a variety of disorders. In adults it has been found to be a risk factor for sensorineural hearing loss (SNHL), although the mechanism currently remains unknown. We investigated the hypothesis that obese children are similarly at increased risk for SNHL.

**Methods:** Cross-sectional data from the U.S. National Health and Nutrition Examination Survey for 1,488 participants ages 12 to 19 years were analyzed. This sample is representative of the non-institutionalized U.S. population. Subjects were classified as obese if their body mass index (BMI) >95th percentile. An average pure-tone hearing level greater than 15 dB for 0.5, 1, and 2 kHz (low frequency) and 3, 4, 6, and 8 kHz (high frequency) was defined as a SNHL.

**Results:** Compared to normal weight adolescents (BMI 5%–85%), being obese was associated with elevated pure tone hearing thresholds and a greater prevalence of unilateral low-frequency SNHL (15.2 versus 8.3%,  $P > 0.01$ ) in bivariate analyses. Obesity was associated with a 1.85 fold increase in the risks of unilateral low-frequency SNHL (95% CI: 1.10–3.13) in multivariate analyses after controlling for multiple hearing-related covariates.

**Conclusions:** These data indicate for the first time that childhood obesity is independently associated with higher hearing thresholds across all frequencies and an almost 2-fold increase in the risk of unilateral low-frequency hearing loss.



## Second-hand Smoke Exposure and Sensorineural Hearing Loss in Adolescents

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**Background:** To investigate the hypothesis that second-hand smoke (SHS) exposure is associated with sensorineural hearing loss (SNHL) in adolescents, a previously unexplored area.

**Methods:** Cross-sectional data from a sample representative of the U.S. non-institutionalized population in the National Health and Nutrition Examination Survey (2005-2006) was analyzed in bivariate and multivariate analyses. Relevant data were available for 1,533 participants 12 to 19 years of age who underwent audiometric testing, had serum cotinine levels available, and were not actively smoking. SNHL was defined as an average pure-tone level greater than 15 dB for 0.5, 1, and 2 kHz (low frequency) and 3, 4, 6, and 8 kHz (high frequency).

**Results:** SHS exposure, as assessed by serum cotinine levels, was associated with elevated pure-tone hearing thresholds at 2, 3, and 4 kHz, a higher rate of unilateral low frequency SNHL (11.8% versus 7.5%;  $p < 0.04$ ), and a 1.83-fold increased risk of unilateral low frequency SNHL in multivariate analyses (95% CI, 1.08-3.41). The prevalence of SNHL was directly related to level of SHS exposure as reflected by serum cotinine levels. In addition, 82% of adolescents with SNHL did not recognize that they had hearing difficulties.

**Conclusions:** This data indicates that SHS exposure is independently associated with elevated pure-tone hearing thresholds and an increased prevalence of low-frequency SNHL that is directly related to level of SHS exposure. Most affected adolescents are unaware of their hearing loss. Thus, adolescents exposed to SHS may need to be closely monitored for early hearing loss with periodic audiologic testing.



## Relationship of Fetal Cord Blood to Maternal Serum Concentration Ratio Of PCB Congeners To Physicochemical Parameters

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**Background:** Polychlorinated biphenyls (PCBs) are ubiquitous, found even in fetuses where they exert deleterious effects on various organ systems during gestation. To reach the fetus, PCBs must cross the placenta. A useful marker of placental-PCB transfer is the ratio of PCB concentration in cord blood versus maternal blood.

**Methods:** We included in the study 1,134 births during the period of 2002 to 2003 from 2 districts in eastern Slovakia known to be highly contaminated by PCBs. Concentrations of 15 PCB congeners (IUPAC No. 28, 52, 101, 123+149, 118, 114, 153, 105, 138+163, 167, 156+171, 157, 180, 170, and 189) in the umbilical cord (C) and maternal serum (M) were determined.

**Results:** The proportion of PCB congeners transferred across the human placenta decreased with increasing octanol-water partition coefficient  $K_{ow}$ .

**Conclusions:** Results for congeners with sufficient percentage of detection showed that C/M ratio was related to the logarithm of  $K_{ow}$ , fusion enthalpy at the melting point, molecular weight, water solubility, total surface area of the molecule, solvent accessible surface area, melting point, molar volume, and molecular electronegativity distance vector. Whereas our focus has been on the physicochemical properties of the individual congeners as predictors of their transfer across the placenta, other factors may influence the maternal to fetal ratio.



## Weight Status and Perception in Assessing Risk of Tobacco Use and Asthma in Adolescents

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**Background:** The urban environment incorporates both pollution and social factors. While rates of asthma and tobacco use are higher in urban environments, no previous study has included weight status and perception in assessing the risk of tobacco use and asthma.

**Method:** The following data was obtained using the 2009 New York City Youth Risk Behavior Survey: body mass index (BMI) using self-reported height and weight, perceived weight, tobacco use in the past 30 days, current tobacco use for 20 in the past 30 days, and an asthma attack in the past 12 months. Cross-sectional weighted analysis accounting for complex survey design was completed using SAS-callable SUDAAN.

**Results:** By BMI, 15.5% were overweight and 11.6% obese. However, by perception, 21.7% were overweight and 3.3% obese. Tobacco users were less likely to perceive themselves as overweight versus non-tobacco users (54.3% vs 60.2%, 95% CI 50.0%-59.0%, 59.1%-61.4%). Current tobacco users were more to perceive themselves as normal weight versus non-current users (28.0% vs 17.4%, 95%CI 20.0%-37.7% 16.4%-18.5%). Adolescents with asthma were more likely to be overweight by BMI than those without asthma (20.9% vs 15.8%, 95%CI 18.0%-24.1%, 14.4%-17.4%).

**Conclusions:** Overweight BMI is associated with asthma while under/normal weight perception is associated with tobacco use. This may be explained by weight misperception among adolescents with asthma who use tobacco or by tobacco use for weight loss. Given the influence of social environment on tobacco use and weight perception, the study of the urban environment, risky behaviors, and health outcomes is a critical part of pediatric environmental health.



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## Children are Walking! Travel Patterns and Safety of Child Pedestrians

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**Background:** Active travel and mobility are integral for a healthy lifestyle. Until recently, there has been little research on the travel patterns of children, in particular during leisure hours. An increasing interest in both the lifestyle and activity levels of children and continuing concern for their safety and a secure environment require more detailed information about trip patterns and activities.

**Methods:** Advanced trip survey tools and methods were tested with children in Israel to study travel patterns and behaviors, as well as exposure to dangers on roads. The survey tools included a self-reported Internet-based travel survey as well as a GPS-based travel survey and follow-up computer-assisted personal interview with children aged 6-12.

**Results:** The findings indicate that children make trips both for school and leisure purposes. Walking is the most common mode of travel, and the children in Israel walk at a higher rate than their counterparts in other developed countries. The study indicated a number of dangerous characteristics in the active travel of children in Israel, including: travel without adult supervision (>36% of the trips were made alone); vehicles not yielding to children at crosswalks; bicycling on roads and without helmets from a young age; lack of safe pedestrian walkways and more.

**Conclusions:** It is important to increase the mobility of children as part of a healthy lifestyle; however, more efforts are needed to determine the dangers to child pedestrians and promote safe walking.



## Assessing Geographic Distribution of Pediatric Cancer Cases and Air-Released Carcinogens Using Cancer Registry and National Pollutants Release Inventory Data

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**Background:** Integrative data approaches to studying environmental causation of pediatric diseases can benefit from the use of public health and environmental databases. This study centers on the use of publicly funded databases to explore geographic collocation of carcinogens emitted by industries to air and childhood cancers in Alberta, Canada between 1994 and 2005.

**Methods:** We created a descriptive geospatial framework at the level of forward sortation areas (FSA), using: (1) data from the National Pollutant Release Inventory on IARC-1 carcinogens emitted into the air; (2) standardized emissions according to benzene's toxic equivalency potential; (3) data aggregated by location and time of children's cancer incidence/population to calculate incidence rates in Alberta; and (4) cumulative distribution of cancer cases and population of children in relation to the distance to nearest emitting facility to establish hypothetical areas of exposure.

**Results:** The annual average of 12 IARC-1 carcinogens emitted to the air was 7,832 benzene-equivalent metric tons, occurring in 20 out of the 150 FSAs in Alberta. Childhood cancer—predominantly leukemia—occurred in 126 FSAs, with an estimated provincial rate of 15.2 cases per 100,000 children. Distance analysis did not show a significant association between incidence rates and proximity to emitting facilities. However, cancer cases accumulated faster than the population of children 3km around emitting facilities.

**Conclusion:** The developed geospatial approach to pediatric cancer occurrences and air-released carcinogens and use of publicly funded databases allowed the creation of a descriptive framework useful for targeting future cause-related studies in identified areas of interest within a 3km of emitting facilities.



## Case of Lead Poisoning and the Impact of Decreased Funding: A Role for the U.S. Pediatric Environmental Health Specialty Units Network

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**Background:** A healthcare professional notified the regional pediatric environmental health specialty unit (PEHSU) regarding a child with blood lead levels (BLL) of 25  $\mu\text{g}/\text{dL}$ . Officials at the local and state health department mentioned that nothing could be done due to lack of resources given the recent loss of funding from the Centers for Disease Control and Prevention. The regional PEHSU determined the exposure source was the father's work in a print shop that used lead ink. The father's screening BLL was  $>100 \mu\text{g}/\text{dL}$ . The Occupational Safety and Health Administration then assessed other shop workers and their children.

**Methods:** A retrospective study analyzed 7,512 total PEHSU contacts between January 2007-December 2012. Seasonal and regional trends in lead contacts were analyzed along with patterns in location of lead exposure, route of exposure, patient geographic location, referral source, patient age and gender.

**Results:** Lead was overwhelmingly the primary topic of concern for which the U.S. PEHSU's were contacted (27%-35%). More than 78.5% of calls or referrals to PEHSU's were from health care professionals. The majority of such calls regarded children aged 2-5 years. The majority of exposures (70%) occurred in homes. This included work exposures being brought home to children. Outreach activities were primarily focused on established health care professional training rather than student/trainee education.

**Conclusions:** Despite significant strides in lead policy and toxicity prevention, lead remains a serious health threat. A significant portion of PEHSU lead contacts were from within the medical and public health community, indicating many lingering care questions. The PEHSU network is a unique and valuable resource for evaluating patterns and should be expanded to include further international members.



## The Role of Pediatricians in Recognizing and Reducing the Health Impact of Environmental Factors

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**Background:** Should pediatricians simply react to symptoms? Or should they seek to know more about patients' environmental determinants and their impact (eg, exposure to endocrine disruptors, pesticides, air pollutants, and electromagnetic fields)? And should doctors proactively raise awareness among the parents of their patients of the dangers of such threats and of how to reduce their impact? When the Respirer Network was formed in Paris in 1994, its 60 member-pediatricians suspected that air pollution could explain the excessive number of respiratory symptoms they saw at certain times of the year.

**Methods:** The network worked with epidemiologists to verify this suspicion.

**Results:** Respirer learned that:

- children are particularly vulnerable to the impact of air pollution;
- effects are dose dependent;
- individuals are not equally exposed.

Respirer saw that:

- scientists' recommendations to health authorities are not always followed by action;
- changing how people think, feel and act takes time and effort;
- pediatricians should not wait for health authorities to ask them to get involved.

**Conclusion:** Respirer believes pediatricians are overloaded with information and thus need simple, clear messages to inform their own actions and those of their patients. The answer is to encourage pediatricians and epidemiologists to interact to better understand and communicate the relevancy of their findings.



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## Children's Environmental Health Trends: The Need for Pediatric Environmental Health Specialty Unit Networks

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**Background:** Pediatric environmental health specialty units (PEHSU) were created in 1998 by the U.S. Environmental Protection Agency (EPA) and the Agency for Toxic Substances and Disease Registry (ATSDR). Currently, there are 12 regional PEHSU sites in the U.S., each affiliated with an academic center and including an environmental medicine physician and pediatrician. The mission of the PEHSU program is to consult with patients or clinicians on environmental hazards, provide referrals and build capacity by educating medical providers on children's environmental health. All contact from the outside community to the PEHSU are recorded and compiled on a quarterly basis. This information provides a novel and unique perspective in gauging the emerging environmental issues facing children's health providers.

**Methods:** A retrospective study analyzed 7,512 total PEHSU contacts between January 1, 2007 and December 31, 2012. Trends in contacts were analyzed by chemical substance along with patterns in location of exposure, caller type, patient geographic location, referral source, patient age and gender.

**Results:** During the study period, lead was overwhelmingly the primary topic of concern for which the PEHSUs were contacted (27% to 35% of the yearly contacts). More than 78.5% of calls or referrals to PEHSUs were from health care professionals. The majority of calls from health care professionals regarded children aged 2 to 5 years. The majority of exposures (>70%) occurred in the home setting.

**Conclusions:** This study demonstrated that a significant portion of PEHSU contacts originate from within the medical and public health community. Moreover, this study showed that the PEHSU network is a unique and valuable public health resource for evaluating patterns in children's environmental health.



## Integrating Dietary and Pesticide Monitoring Data to Assess Pesticide Uptake Among Israeli Children

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**Background:** This research quantifies the potential dietary uptake of pesticide compounds among a group of Be'er Sheva-based children aged 4-7 years.

**Methods:** With a focus on consumption of fruit and vegetables, it merges the results of pesticide monitoring programs of the Israel Ministries of Health and Agriculture (2006-2010) with food frequency and 24 recall surveys conducted by Ben Gurion University's School of Nutrition (2008-2010). The resulting dietary uptake profile is used to assess conformance with regulatory standards for individual food items and pesticide compounds mandated by the Ministry of Health. A comparison is made with the results of the ministry's Risk Assessment for Israeli adults. Cumulative risk assessment is also conducted for organophosphate compounds because of their association with a range of detrimental health effects and in light of changes in regulation that will restrict their use in Israeli agriculture through 2016.

**Results:** While most consumption conforms to regulatory standard, several compounds exceed ADI on a per food basis or in aggregate (i.e. for the fruit and vegetables assessed). The proportion appears to be greater than that for the adult population. This result is magnified on a cumulative basis.

**Conclusion:** The probability that children's diet has a higher risk of exceeding standards dictates a re-examination of the adequacy of current regulation for protecting children. While protecting the food supply at source through better regulation, monitoring and enforcement is a priority, the issue of informed consumer choice also needs to be considered to provide the basis for switching less risky items for more risky ones.



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## New Sources for Data on Children and Air Pollution

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**Background:** Children are particularly sensitive to outdoor air pollution because they spend many hours outside. In fact, air pollution affects their health even before birth. Traditional data sources on the impact of air pollution mainly capture hospitalizations and mortality. Epidemiologists don't make findings sufficiently meaningful to those who need to act.

**Methods:** We reviewed the most recent epidemiological findings on children and outdoor air pollution. Through the European Commission's Syndromic Surveillance Systems (Triple-S) project, we searched for new data sources that better capture acute effects of air pollution on children's health. We sought answers to the key question of how to better communicate epidemiological findings to health practitioners, schoolteachers and others through data from the commission's Aphekom project.

**Results:** Air pollution impairs the development of children's respiratory capacity, and is associated with new cases of asthma, exacerbation of existing conditions and school absences. In 10 European cities, living near busy roads increased the incidence of asthma in children by 15%. And prenatal exposure to air pollution may not only cause pre-term delivery and low birth weight but may also affect brain development. The Triple-S project shows the value of using pre-diagnosis data to better capture the acute effects of air pollution on children's health, thus complementing traditional data sources for this impact.

**Conclusions:** New data sources can help better understand air pollution as a major health determinant of children's health. The challenge for epidemiologists now is to work closer with health and school professionals, and to help urban planners foster better air quality environments.



## Preliminary Steps in Understanding and Reducing Children's Exposures to Pesticides and Other Hazardous Chemicals in Israeli Schools and Kindergartens

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**Background:** A preliminary assessment of young children's exposure to pesticides and other hazardous chemicals in Israeli rural and urban pre-schools and kindergartens found low awareness of risk or solutions, and significant differences between Israeli and U.S. facilities, climate control and cleaning practices, regulations. Differences also existed between pesticide exposure studies in terms of frequency, timing and type of pesticide use, and pesticide residues detected.

**Methods:** In response to the low awareness in Israel, 2 projects were conducted in 2013 for the Ministry for Environmental Protection, and 2 current kindergarten programs are underway to assess needs, develop policies and provide education. The education programs were implemented in Jewish and Bedouin schools.

**Results:** Outcomes include survey and inspection data, a synthesis of relevant Israeli sanitation and building guidelines and U.S. experience, educational materials for schools and kindergartens, recommendations for new pesticide use regulations in childcare and school environments, and guidelines will be formatted for Haifa Bay kindergartens based on the kindergarten studies.

**Conclusion:** This presentation assesses Israel's current awareness and experience in reducing children's exposures to pesticides and cleaning/disinfectant products in pre-schools and elementary schools



## Nutritional Deficiencies Among HIV-Infected Children

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**Background:** Poor nutrition has been associated with impaired immunity and accelerated disease progression in HIV-infected children.

**Methods:** We surveyed HIV-infected Tanzanian children enrolled in a pediatric care program that provided routine nutritional counseling and vitamin supplementation. We obtained anthropometric measurements and determined 24-hour macronutrient and micronutrient intakes and food insecurity. Values were compared to recommended nutrient intakes based on age and gender.

**Results:** We interviewed 48 children ages 2 to 14 years, 60% female, with a median age of 6. The median weight-for-height z-score for children  $\leq 5$  years was 0.69 and BMI-for-age z-scores for children  $> 5$  was -0.84. Values for CD4% were:  $\leq 15\% = 15$  (31%), 16-25% = 16 (33%) and  $> 25\% = 17$  (35%). Macronutrient evaluation showed that 29 (60%) children were deficient in dietary intake of energy; deficiency was more common in older children ( $p = 0.004$ ). Micronutrient evaluation shows that over half of study subjects were deficient in dietary intake of vitamin A, vitamin D, vitamin E, thiamine, riboflavin, niacin, folate, vitamin B12, and calcium. Food insecurity was reported by 20 (58%) caregivers.

**Conclusions:** The diets of many HIV-infected children at the Dar Dar pediatric care program in Tanzania do not meet recommended levels of macro- and micro-nutrients despite nutritional counseling. Enhanced dietary counseling and provision of macro- and micro-nutrient supplements will be necessary to achieve optimal nutrition for most HIV-infected children in resource-poor regions.



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## Air Quality and Objective Health Parameters in European Classrooms

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**Background:** Indoor air quality and health of pupils in schools from 25 European nations was assessed in a project funded by the European Public Health Agency.

**Methods:** A major objective of the project was the harmonization of ambient and health monitoring; personnel involved in data collection underwent multiple training sessions. The health of students determined by both questionnaire and medical examination.

**Results:** Despite the fact that, in questionnaires, pupils and parents reported sensitivity to indoor air quality markers, only a few objective health end-points were significantly associated with air quality. Ambient monitoring uncovered, among others, fine particles (PM<sub>2.5</sub>), carbon monoxide, carbon dioxide, radon, polycyclic aromatic hydrocarbons, formaldehyde and various volatile organic compounds. The tear-film stability (break-up-time) was significantly affected by a number of air quality indicators, but for several other end-points, the association was no longer significant after controlling for potential confounders and multiple clustering.

**Conclusion:** Air quality in European schools is still an issue as indicated by the high variability in this large sample. As the measurements mostly reflect short-term exposures and effects, it seems that subjective symptoms are more sensitive than objective clinical measures of health.



## Atopy as a Risk Factor for the Development of Asthma in Young Recruits: A Retrospective Cohort

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**Background:** The natural history of asthma is a result of the interaction between the disease's genetic basis and environmental factors. Atopy was found as the single most important risk factor for the development of the disease. In recent years, there has been a growing interest in the fraction of adult-onset asthma that can be related to exposures at the working environment. Atopy was consistently found as a risk factor for occupational asthma, although the association level is generally low. Military service in combat units tends to expose cases of mild asthma or cause the de-novo appearance of asthma in a previously healthy young adult. The purpose of the study is to examine the association of atopic background and military occupation to the incidence of adult-onset asthma.

**Methods:** In this retrospective cohort study we included all soldiers drafted to the Israeli defense forces. The medical history of the conscripts during a 3-year follow-up was documented in a computerized database. Medical examinations by pulmonary specialists and exercise testing were performed in all cases of suspected asthma. We examined the incidence of asthma in relation to atopic background at induction (allergic rhinitis, allergic conjunctivitis, atopic dermatitis and contact dermatitis) and military occupation.

**Results:** The study included 128,591 soldiers. Asthma incidences during the 3-year surveillance period were found to be 1.54%. The relative risk for the development of asthma was significantly higher in soldiers occupied in clerical tasks than in those serving in maintenance and combat units (RR of 1.76 and 2.58, respectively,  $p < 0.001$ ). The relative risk for asthma in subjects with atopic disease was found as 1.7. Out of diseases examined, only allergic rhinitis was found as a risk factor. Significant association was found between atopic background, occupation and incidence of asthma. Higher incidence of asthma was found in combat and maintenance units in association with atopy (odds ratio 2.57 and 1.4, respectively). No association existed between atopy and asthma in subjects occupied in clerical tasks.

**Conclusion:** Atopy and, in particular, allergic rhinitis are risk factors for de-novo appearance of asthma in young adults. Atopic background has a significant effect in combat and maintenance units but not in soldiers performing clerical tasks. Atopy is a significant risk factor for the appearance of occupation-related asthma.



## Industrial Projects with a Potentially High Impact on Environmental Health: can Pediatricians Help in the Mediation Process?

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**Background:** Pediatricians are persons of trust in the field of children's environmental health (CEH). Are they also experts in CEH risk evaluation and communication? Can they serve as "information brokers" between stakeholders?

**Methods:** We review the activities of Kinderumwelt, a pediatric not-for-profit agency engaged in CEH since 1991, concerning industrial projects, comprising formal scientific opinions of the commission, scientific papers, essays, public hearings and memberships in federal commissions, and web activities. During the last decade Kinderumwelt was engaged in the public discussion of the following topics:

- Leukaemia in the vicinity of nuclear power plants in Germany;
- Low frequency magnetic fields and leukaemia (e.g. high voltage power lines);
- High frequency electromagnetic fields related to mobile communication;
- Fracking technology;
- Carbon monoxide pipelines in Germany;
- Bisphenol A debate.

**Results:** Why was pediatric mediation/intervention in some cases successful?

- Competence & interdisciplinary approach;
- Pediatric authority and external perception of Kinderumwelt as an independent body;
- Individual and tailored advice to patients/clients, to self-help groups and civil initiatives;
- Use of visualization techniques (e.g. high frequency fields, human biomonitoring, dose-response curves).

Why was pediatric mediation/intervention in some cases not successful?

- Mediation/intervention occurred at a very late stage;
- Individuals or groups applied alternative concepts, e.g. "intuitive toxicology" and "all-or-none response curves" instead of dose-response curves;
- Existence of large deviations in concepts of acceptable/non-acceptable risks between advocacy groups and pediatricians/Kinderumwelt;
- Use of scientific studies and data for campaigning instead of fair discussion between activists and Kinderumwelt.

**Conclusion:** There is a role for pediatricians and organizations such as Kinderumwelt in the CEH field. A web-based forum or database on best practice examples and experiences would be desirable. In fact, we



believe that the discussion on priorities in CEH issues should be intensified ([www.allum-europe.eu](http://www.allum-europe.eu) is offered as an example for this purpose).

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## Respiratory Hospitalizations of Children Living Near a Hazardous Industrial Site Adjusted for Prevalent Dust: A Case-Control Study

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**Background:** The Ramat Hovav Industrial Park (IP), located in southern Israel, hosts 24 chemical industry facilities and the national site for treatment of hazardous waste. Yet information about its impact on the health of local population has been mostly ecological, focused on Bedouins and did not control for prevalent dust storms. This case-control study examined whether living near the IP could lead to increased risk of hospitalization for respiratory diseases.

**Methods:** Children <14 years of age living within 40 km of the IP who were hospitalized for respiratory illnesses were compared to children admitted for non-respiratory conditions. Individual exposures were based on residential proximity to the IP. Associations between hospitalization and exposure to IP pollution were examined for three age groups (<1, 1-5, 6-14) controlling for important covariates and particulate matter (PM) with aerodynamic diameter <10  $\mu\text{m}$  (PM<sub>10</sub>).

**Results:** We found evidence for increased risk of respiratory hospitalization with proximity to the IP for infants in the first year of life (OR: 2.41, 95% CI: 1.46-3.97). Regional PM<sub>10</sub> was associated with an overall increased risk (OR: 1.03, 95% CI: 1.01-1.06), based on PM<sub>10</sub> interquartile range. In models with both distance from the IP to residence and PM<sub>10</sub>, the estimate for infants aged <1 year was smaller but still significant (OR: 1.99, 95% CI: 1.12-3.55).

**Conclusion:** Residential proximity to a hazardous industrial site may contribute to early life respiratory admissions, beyond that of prevailing PM<sub>10</sub>.



## Respiratory Hospitalizations of Children and Residential Exposure to Traffic Air Pollution in Jerusalem

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**Background:** Although exposure to traffic-related air pollution has been reported to be associated with respiratory morbidity in children, this association has not been examined in Israel. Jerusalem is ranked among the leading Israeli cities in transport-related air pollution. This case-control study examined whether pediatric hospitalization for respiratory diseases in Jerusalem is related to residential exposure to traffic-related air pollution.

**Methods:** Cases of Jerusalem residents aged 0-14 years hospitalized for respiratory illnesses between 2000 and 2006 were compared to children admitted electively or urgently for non-respiratory conditions. Individual exposures were measured as distance from residence to nearest main road, the total length of main roads, traffic volume, and bus load within buffers of 50-, 150-, and 300-meters around each address.

**Results:** Cases were more likely to have any bus traffic passing within 50m of their home (OR: 1.16 and 1.10, 95% CI: 1.04-1.30 and 1.01-1.20 for elective and emergency controls, respectively). Girls aged 5-14 years who lived within 86m of a main road were at increased risk of respiratory admission when compared to emergency controls (OR: 1.13,  $p = 0.05$ ). Our findings indicated that older girls (5-14) who had main roads and heavy traffic within 150m of their residence had higher risks of respiratory hospitalization, although most estimates did not reach statistical significance.

**Conclusion:** Exposure to bus traffic within 50m of residence may contribute to childhood respiratory hospitalization. Older girls are possibly at higher risk of respiratory hospitalization associated with traffic-related pollution.



## Umbilical Cord Blood Cell Proliferation as a Sub-clinical Endpoint in Relation to Environmental Exposures: a Biomonitoring Pilot Study

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**Background:** An adverse effect of air-pollution on cell physiology supposedly involves impairment of cell oxygenation and its proliferation process. We assessed the cell proliferation (CP) ratio of lymphocytes in umbilical cord blood as an indicator of a subclinical pathology in the fetus that might be specific to environmental factors.

**Methods:** We enrolled 346 Arab-Bedouin women giving birth in a local hospital. A questionnaire and cord blood samples were collected. This population is featured by high rates of birth anomalies and multiple environmental exposures, originating from a local industrial park, frequent male smoking and open bonfire usage. Samples were maintained at +2°C and tested by MTT cell proliferation assay within 48 hours.

**Results:** Average CP ratio was  $2.46 \pm 1.3$ ,  $Me=2.1$ , (0.7-8.8). Women in the first and fourth quartiles of the CP ratio reported higher rates of using ventilator cooling systems and stoves without chimneys, respectively. Women in the 4th quartile frequently lived in shacks or single-level buildings, used open fires or stoves without chimneys for heating and cooking, and had more complaints about nearby traffic (67.0% vs. 53.0% in first quartile,  $p=0.05$ ). CP ratio was lowest in newborns with major anomalies ( $2.24 \pm 0.99$ ,  $n=10$ ), followed by the ratio among newborns with minor anomalies ( $2.34 \pm 1.21$ ,  $n=12$ ), and both were lower compared to healthy newborns ( $2.47 \pm 1.33$ ,  $n=324$ ). This disparity may reflect a different pathophysiology for minor and major anomalies.

**Conclusions:** Proliferation of cord blood cells might be considered as an early subclinical indicator of birth anomalies, sensitive but not specific to environmental exposures.



## High-Dose Methotrexate Administration in Pregnancies Misdiagnosed as Ectopic

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**Background:** Ectopic pregnancy, accounting for about 2 percent of all pregnancies, is the leading cause of first-trimester maternal death. Medical termination of ectopic pregnancy with methotrexate, a major human teratogen, has more than tripled in the United States during the last decade (from 11% in 2002 to 35% in 2007), as it minimizes the risks, complications, and costs associated with surgical terminations. However, diagnosing an early ectopic pregnancy remains difficult despite advances in imaging. This may result in untoward exposure of healthy fetuses to a major teratogen during critical stages of embryogenesis, due to medical errors

**Methods:** We report the outcomes of all subjects who sought consultation after exposure to high-dose methotrexate to induce abortion in presumed ectopic pregnancies, which were later identified as viable intrauterine pregnancies by 3 North American teratology information services between 2002 and 2010.

**Results:** Eight women with normal, desired pregnancies were administered high-dose methotrexate in the first trimester because of presumed, misdiagnosed ectopic pregnancies. All pregnancies resulted in catastrophic outcomes. Two pregnancies resulted in severely malformed newborns with methotrexate embryopathy; 3 women miscarried shortly after exposure, and the erroneous diagnosis led physicians to advise and perform surgical termination in 3 cases.

**Conclusion:** Erroneous diagnosis of intrauterine pregnancies as ectopic with subsequent first-trimester exposure to methotrexate resulted in the birth of severely malformed babies or fetal demise.



## Attention Deficit/Hyperactivity Disorder in Schoolchildren from an Agricultural Environment

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**Background:** Reversible in-season neurobehavioral changes were previously observed from 1984 to 1991 in agricultural workers and residents exposed to organophosphorous (OP) pesticide drift in kibbutzim in the Hula Valley, Israel. We assessed the prevalence of Attention Deficit/ Hyperactivity Disorder (ADD/ADHD) in: (1) Family members of participants in the original cohort (n=139), 87 (62.5%) of whom still reside in the same kibbutzim and are exposed to seasonal OP drifts; (2) schoolchildren in the same kibbutzim, 8-12 years-old (n=135), 84% of whom are “second generation” of OP exposures (at least 1 parent has lived >30 years in the valley).

**Methods:** Interviewed families in the original cohort for health problems and prevalence of ADD/ADHD. Also interviewed teachers and parents for health problems, ADD/ADHD and behavioral patterns at school and home. OP exposures (high, low and minimal) were estimated in the schoolchildren.

**Results:** Among the 245 siblings of the respondents in the original cohort, 61 (25%) were diagnosed with ADD/ADHD. There was a strong association ( $p=0.03$ ) between the estimated level of OP exposure and ADD/ADHD in these children. Familial prevalence of ADD/ADHD in the highly-exposed group was higher than in the minimally-exposed group ( $p<0.1$ ; OR=2.6; 95% CI (0.79-8.53)). There was a suggestion of familial prevalence of ADD/ADHD observed in children residing <50 meters from fields (5 of 11; 45%) compared with children residing more distantly (19 of 62; 30%).

**Conclusion:** ADD/ADHD prevalence was associated with estimated OP-exposure. ADD/ADHD in this population exceeded the reported prevalence (5%-7%) in Israel. We postulate that prolonged environmental exposure to OP increases the risk for ADD/ADHD.



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## Pediatric Environmental Health Specialty Units: A Model for Global Implementation

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**Background:** Pediatric environmental health specialty units (PEHSUs) were initially created in the U.S. in the late 1990s. There are now 10 units in the country, and several units have also been created in other nations, including Mexico, Spain and Canada. PEHSUs require an individual with medical expertise and a willingness to learn about children's environmental health, a computer with an Internet connection and a phone. In other words, PEHSUs do not require very expensive equipment that requires exacting conditions to maintain them.

**Methods:** This presentation will review the training, equipment, budget and other resources necessary to create a PEHSU. The international collaborative network for mutual support among PEHSUs will also be described as new units would be advised to avail themselves of this network for continuing education, consultation about unfamiliar toxicants and other forms of collaboration.

**Conclusions:** PEHSUs can be implemented virtually anywhere in the world.

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## Prospective Cohort Study of Developmental Origins of Adult Diseases in the Slovak Population (PRENATAL) – First Information

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### Acknowledgements:

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**Background:** The in utero environment is sensitive to environmental stressors and plays an important role in determining future susceptibility to a number of diseases. A longitudinal epidemiological project was



launched in the Slovak Republic in 2010, aimed at assessing health and environmental factors significant in the development of metabolic, endocrine and cardiovascular diseases later in life.

**Methods:** The project involves approximately 900 mother-child dyads from 8 Slovak regions. Pregnant women were recruited at the beginning of pregnancy. Information on health status was gathered via questionnaire, together with data on environmental exposures and diet before and during pregnancy. Samples of maternal blood, cord blood and breast milk are currently being collected for analyses of metabolic parameters and assessment of prenatal and early postnatal exposure to selected environmental pollutants, including PCBs, pesticides, perfluoroalkyl compounds and toxic metals. Children will be followed up to the age of 3 years.

**Results:** Out of 1,495 pregnant women approached about cooperation, 23.5% (352) refused to participate in the project. After excluding spontaneous abortions later in the pregnancy, 1,083 women were finally included in the follow-up. So far, 746 newborns were born within the PRENATAL project and follow-up is ongoing.

**Conclusions:** Prospective birth cohort studies represent a promising approach towards testing various hypotheses on early life risk factors for the development of obesity and adult diseases.

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## Effectiveness of Washing for Removing Pesticides from Fruit

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**Background:** Chronic, low-level exposure to pesticides in children may be linked to pediatric cancer, and neurodevelopmental disorders such as attention deficit disorder. Diet is a major source of exposure, with pesticide-sprayed fruit often a dietary component that children are encouraged to consume in place of processed, high-carbohydrate snacks. Thus, ways to remove pesticides from treated fruit would be useful to lower children's exposure.

**Methods:** Apples treated with pesticides were obtained from the Rutgers University Agricultural Extension farm. Five different removal treatments that can readily be done by consumers were evaluated: (1) no treatment; (2) 15 seconds of wiping with a paper towel; (3) washing with lemon/juice/vinegar/ water solution; (4) 1% soap solution; and (5) commercially available vegetable wash. Apples were then wiped and rinsed for 1 minute. The pesticide residue was extracted from the apple using 100 mL of ethyl acetate, concentrated to 2 mL and analyzed by GC/MS.



**Results:** The levels of pesticide measured per apple on the untreated fruits were Captan  $23.1 \pm 1.9 \mu\text{g}$ , Imidan  $7.0 \pm 1.7 \mu\text{g}$ , Fenprothrin  $15.1 \pm 1.6 \mu\text{g}$ . All treatment methods reduced Imidan levels  $>50\%$ . For Captan, the soap solution (39%) and VeggiWash® (51%) were more effective. Only a modest reduction in Fenprothrin residue ( $\sim 10\%$ ) was observed across all treatments.

**Conclusion:** Some, but not all pesticides can be removed from apples by washing and wiping of fruit. While washing and wiping are recommended, more effective methods are needed to reduce children's dietary pesticide exposure.

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## Center Support for Children's Environmental Health in Milwaukee

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**Introduction:** The Children's Environmental Health Sciences Core Center (CEHSCC) supports research and community engagement related to the environmental determinants of childhood diseases. Members come from regional research universities, a major medical school, and a new school of public health. They work along the translational arc from molecular and cellular experimentation to animal research and studies with children in the community and clinic.

**Methods:** Scientists are supported by 3 research cores. One provides infrastructure to study developmental toxicology in the zebrafish model, including aquatic animal facilities, a neurobehavioral toxicology laboratory, and staff to conduct genome modification procedures. Another offers advanced imaging and histology, clinical laboratory testing, (epi)genomic sequencing and analysis, biobanking of human and animal samples, and broad exposure analysis capability. The third focuses on studies with children, providing in-depth epidemiological support in community and clinical settings, consultation in biostatistics for all members and bioinformatics expertise related to genomic sequencing data.

**Results:** Examples of research conducted by center members include (1) studies using the zebrafish as a model of mammalian development to understand the developmental toxicology of nicotine; and (2) neurotoxicology related to freshwater exposure to selective serotonin reuptake inhibitors. The center also sponsors a major high school science program linking experimentation with aquatic organisms to teen environmental health issues and works in the Milwaukee community to elevate children's environmental health as in its lead (Pb) and noise pollution initiatives.



**Conclusions:** The center provides a robust structure to support regional scientists in research and community engagement related to children's environmental health.

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## Application of a Biokinetic Model to Estimate the Effectiveness of Different Soil Remediation Scenarios for Lead Contamination

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**Background:** Approximately 40,000 children in Shymkent, Kazakhstan are affected by long-term lead contamination of the environment around a lead smelter. We demonstrate the specificity and effectiveness of applying a biokinetic model (IEUBK) for planning scenarios of soil remediation.

**Methods:** Using a portable device, 156 children in kindergartens/orphanages/daycare centers at different distances from the smelter were tested for blood lead levels. Soil and indoor dust samples were also analyzed using a portable XRF spectrum analyzer. Soil samples were tested for lead bioavailability. Air samples were collected using personal industrial hygiene sampling pumps. IEUBK software was run using different assumptions.

**Results:** Mean blood lead levels ranged from  $7.72 \pm 1.6$   $\mu\text{g}/\text{dL}$  to  $27.7 \pm 1.8$   $\mu\text{g}/\text{dL}$  and correlated with the distance from the smelter. IEUBK model effectively predicted blood lead distribution for all locations ( $r=0.996$ ,  $p=0.003$ ) assuming 50% lead uptake and soil/dust injection factor of 70 to 30. Based on IEUBK combined with Monte-Carlo simulation, it was confirmed that the remediation scenario with cleaning up lead to 250 mg/kg and indoor dust to 290 mg/kg would ensure that 95% children have blood lead levels of less than 10  $\mu\text{g}/\text{dL}$ .

**Conclusions:** We demonstrated that calibrated IEUBK allows prediction of children's blood lead levels in a wider range of parameters than that supposed by its authors. The approximation of IEUBK as a set of multiple regressions allowed us to reverse the model and combine it with statistical simulations. The model can be recommended for the further monitoring of environmental and health issues in Shymkent for effective remediation planning.



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## Pediatric Environmental Health Specialty Units: The Experience of the Southeast PEHSU

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**Background:** The U.S. Southeast Pediatric Environmental Health Specialty Unit (PEHSU) is located in Atlanta, Georgia, serving Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee. Like all the other PEHSUs, it provides information, technical assistance and training for professionals and the public.

**Methods:** The SE PEHSU has unique characteristics determined and defined by the composition of the leadership team, its geographic location and the environmental conditions of the region, and by the specific challenges and opportunities that arise. The PEHSU actively collaborates with other organizations to expand its network locally, regionally, nationally and internationally. It worked with the U.S. Environmental Protection Agency (EPA) and the Agency for Toxic Substances and Disease Registry (ATSDR) in a small mining town in rural Alabama raising awareness of environmental justice issues. The SE PEHSU has also developed a collaboration with colleagues in Santiago, Chile.

**Results:** The collaboration in Alabama has resulted in an internationally recognized project to reduce environmental health disparities and now engages participants from throughout the U.S. and internationally as well. The collaboration with colleagues in Chile has resulted in multiple academic exchanges.

**Conclusions:** The SE PEHSU team, the PEHSU network and the field of children's environmental health have been significantly enriched by the range of experiences and lessons of the SE PEHSU and even more so by the cumulative experiences of all the PEHSUs.



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## Break the Cycle of Environmental Health Disparities: An Interdisciplinary Program

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**Background:** Children who grow up in circumstances of social and economic disadvantage are exposed to a variety of environmental factors that can result in serious childhood health problems. In the developing world, these are: food shortages, susceptibility to infectious disease and exposure to conflict and violence. In industrialized countries, they are exposed to toxins from industry and motor vehicles, dilapidated homes and violence in their neighborhoods. These adverse conditions result in increased morbidity and mortality and are termed Environmental Health Disparities.

**Methods:** Break the Cycle of Environmental Health Disparities is an interdisciplinary program offered by Emory University. The program guides students through the development and completion of projects focused on alleviating these disparities, and requires that they present their work at a conference and write a paper for publication.

**Results:** To date, we have had 8 annual programs with more than 60 students from more than 20 universities and disciplines in 8 states in the USA, and 1 from a Latin American country, with 5 published monographs in international journals and 1 in press.

**Conclusion:** We will present the model, the process and examples of projects, as well as a survey of past participants and discuss possible replication elsewhere in the world.



## Assessing the Impact of a Fortified Supplementary Food on the Health of Children in Day Care in South Africa

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**Background:** South Africa's children, particularly those in poor environments, suffer from micronutrient deficiency that impacts their health. Addressing undernutrition in poor environments is essential.

**Methods:** This study evaluated the impact of e'Pap, a fortified food, on the health of a cohort of 66 children in Alexandra, Johannesburg: 33 males and 33 females with a mean age of 4.6 years. Data collection took place between September and December 2010. All participants were de-wormed at baseline. Participants were given e'Pap (50 g) twice daily at the daycare centers and returned for 2 subsequent data collections, 1 month apart. Height, weight, mid-upper arm circumference and handgrip strength was measured. Bioelectrical impedance analysis (BIA) was performed to derive lean body mass. Serum levels of zinc, iron, selenium, vitamin A, vitamin D and albumin were measured. Seven community health workers were trained to administer the questionnaires, do measurements and record data.

**Results:** Food insecurity was relatively high (57%) among children as reported by parents/guardians. Lean body mass, as measured by bioelectrical impedance, showed a consistent increase. BIA reflected a slight but consistent improvement of the illness marker among the children. Blood analysis showed that 32%, 40% and 6% of children had selenium, iron and zinc levels, respectively, below the normal range. Increases in all micronutrients after 3 months, with the exception of vitamin D, were observed.

**Conclusion:** Despite the short period of intervention, there were statistically significant improvements in key micronutrient levels, handgrip strength and the BIA Illness Marker. The results indicated a beneficial effect of e'Pap.



## Dioxins/PCBs and Pubarche among Russian Boys in a Longitudinal Study

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**Background:** Although several studies have examined the impact of environmental exposures on puberty, there are few studies on their association with pubarche.

**Methods:** To evaluate the association of polychlorinated biphenyls (PCBs), and dioxins with pubarche among boys in an industrial town with a wide range of exposure, boys in Chapaevsk, Russia were enrolled at ages 8-9 years and followed annually for 3 years by a single physician. Their pubertal development was determined via serial collection of data and biological samples. Exposures were measured on enrollment samples. We computed individual and summed lipid-adjusted concentrations for dioxin/PCBs congeners. Cox proportional hazards models were fit for time to onset of pubarche (defined as pubic hair stage 2 [P2] or greater on the Tanner Scale), along with interval censored models for mean age at onset of pubarche, adjusting for confounders.

**Results:** Of the 310 boys enrolled at age 8 years, 4% (n=11) had onset of pubarche. This increased to 10% at 9 years (46 of 476) and 39% at 12 years. In multivariable Cox models, age at onset of pubarche was significantly earlier with higher caloric intake, taller height, and greater BMIs at baseline. In interval censored models for age at pubarche adjusted for potential confounders, the highest quartile of serum TCDD as well as highest quartile of  $\Sigma$ PCBs was associated with ~15 months earlier onset of P2.

**Conclusion:** Our data suggests that TCDD and PCBs may be associated with earlier onset of pubarche and will be further examined in this cohort.

## Exposure to Environmental Tobacco Smoke and the Health of Slovak School Children

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**Background:** Environmental tobacco smoke is a serious factor of indoor air pollution and has influence on children's health. The aim of the project is to analyze the problems of passive smoking and health in Slovak school children.

**Methods:** The status of physical and psychological health of children in relation to exposure to tobacco smoke was examined in the representative group of 1,070 children aged 6-15 years, with an equal number of boys and girls. The standard methods included anonymous questionnaires filled in by parents, checklist individual strength (CIS) validated questionnaires, brief pain inventories (BPI), and anthropometric variables. The SAS program was used for statistical analysis.

**Results:** The prevalence of passive smoking in Slovak children is significantly higher in big cities (27%). There was a significant relationship between exposure to second-hand smoke and the age of children, socio-economic status, incompleteness of the family and the level of parental education. Significantly higher prevalence of respiratory diseases in children exposed to passive smoking was shown. Children exposed to second-hand smoke had less healthy living habits, in terms of nutrition and levels of physical activity. The relationship between passive smoking and body composition of children was not significant, nor were the relationships between ETS and emotional disorders (CSI score) and behavioral functions (BPI score).

**Conclusions:** Results confirmed the impact of exposure to ETS on health status and health behavior of school children. Our study revealed a lack of intervention in the area of the protection of children from exposure to toxic tobacco smoke.



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## The Effects of the Built Environment on Childhood Asthma in North Texas

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**Background:** The effect of the built environment on childhood asthma prevalence was explored in 2 types of counties in Texas: urban and rural. Particular features of the built environment, including parks, major highways, toxic release inventory (TRI) facilities, and neighborhood safety were examined for their influence on childhood asthma.

**Methods:** Respondent data from the Center for Children's Health 2012 Community-wide Children's Health and Planning Survey was used to compare the prevalence of children with asthma in Tarrant and Parker counties using Geographic Information Systems and IBPM SPSS software as tools for proximity and statistical analysis, respectively.

**Results:** There were comparable percentages of children with asthma living in urban versus rural environments. Parents of children suffering from and hospitalized due to asthma were found to have lower incomes and education levels. The homes of children hospitalized due to asthma were on average located closer to parks and TRI facilities than those not hospitalized.

**Conclusions:** The greater number of children hospitalized due to asthma among those living closer to TRI facilities appears to show that this feature of the built environment poses one of the more negative impacts on children with asthma.



## Dimercaptosuccinic Acid Chelation in Children $\leq 5$ Years with Severe Lead Poisoning in Zamfara, Nigeria

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**Background:** In 2010, Médecins Sans Frontières (MSF) discovered lead poisoning on an unprecedented scale in northern Nigeria. The U.S. Centers for Disease Control and Prevention (CDC) confirmed the source as contamination from artisanal gold mining and refining of gold from lead-rich ore. We report on the effectiveness and safety of 3,180 courses of dimercaptosuccinic acid (DMSA) chelation, the largest series reported to date.

**Methods:** Courses of DMSA of 19- or 28-day duration given from June 2010 to June 2011 to children  $\leq 5$  years with initial venous blood lead level (VBLL)  $\geq 45\mu\text{g/dL}$  were included. Effectiveness of DMSA is reported as end-course VBLL as a percentage of pre-course VBLL (ECP). Lower ECP is desirable.

**Results:** Of 3,180 DMSA treatment courses administered to 1,156 children, 28% were first ever courses. Courses per patient ranged from 1 to 15. Thirty-three percent and 7% of courses had a pre-course VBLL  $\geq 80\mu\text{g/dL}$  and  $\geq 120\mu\text{g/dL}$ , respectively. Overall, ECP had a geometric mean of 74.5% (95%CI 69.7,79.7); for all 19-day courses (n=3120) ECP was 77.2% (95%CI 70.5,80.3) and for 28-day courses (n=60, all inpatients), ECP was 38.8% (95%CI 32.4,46.4). ECP was significantly lower in older children, first-ever treatment courses, courses with a longer gap since a previous course, courses with a greater proportion of doses directly observed and with higher pre-course VBLL. No clinically significant adverse effects were detected.

**Conclusion:** Oral DMSA as a single therapy is safe and effective for children with life-threatening lead poisoning. Factors associated with a greater percentage decline in VBLL included a higher pre-course VBLL and treatment in the inpatient setting.



## The Human Early-Life Exposome Project—Integrating Early-Life Environmental Exposures and Child Health Across Europe

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**Background:** Research on the vulnerability of the developing fetus and neonate to environmental exposure generally focuses on single exposure-health effect relationships. The “exposome” concept encompasses the totality of exposures from conception onwards, complementing the genome. A challenge is to broaden the range of exposures usually considered, without increasing exposure misclassification. HELIX (Human Early-Life Exposome) is a new research project aiming to: 1) implement novel exposure assessment and biomarker methods to characterize early-life exposure to multiple environmental factors; and 2) associate these with child health outcomes, characterizing the early-life exposome.

**Methods:** Using 6 existing European birth cohort studies, HELIX will estimate prenatal and postnatal exposure to a range of chemical and physical exposures. Exposure models will be developed for 32,000 mother-child dyads and biomarkers will be measured in a subset of 1,200. Nested repeat-sampling panel studies (N=150) will collect data on biomarker variability, using smartphones and personal monitors to assess mobility, physical activity and exposure to air pollutants, noise, and UV radiation. Omics techniques will determine molecular profiles (metabolome, proteome, transcriptome, epigenome) associated with exposures. Statistical methods for multiple and combined exposures will provide exposure-response estimates for fetal and child growth, obesity, neurodevelopment, respiratory outcomes. A health impact assessment exercise will evaluate risks and benefits of combined exposures.

**Conclusions:** HELIX is one of the first attempts to describe the early-life exposome of European populations and unravel its relation to omics markers and health in childhood. As proof of concept, it will form an important first step towards the life-course exposome.



## Reduction of Levels of Selected Persistent Organic Pollutants Measured in Human Milk

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**Background:** Persistent organic pollutants (POPs) are man-made organic non-volatile compounds, resistant to environmental degradation through chemical, biological, and photolytic processes. POPs were used as pesticides and in industrial processes to produce solvents, polyvinyl chloride, and pharmaceuticals. Human exposure to POPs has been associated with cancer, endocrine disruption, poor reproductive outcomes and insulin resistance. Human milk, with its high fat content, is a preferred matrix for monitoring POPs exposure.

**Methods:** Guidelines from the World Health Organization (WHO) were used to gather samples of human milk. Primiparous women aged 23-35, living in Israel for the last 10 years were recruited from 3 maternity hospitals. Breast milk samples from 52 women were collected between 3-17 weeks postpartum. A pooled sample analysis was performed in the WHO reference laboratory.

**Results:** Many indicator compounds (chlordanes, DDT compounds, hexachlorocyclohexanes and PCBs) were found in detectable levels mostly lower than those reported in European countries. Compared to the previous 1985 survey in Israel, levels have declined significantly. Total PCBs concentration was 23.9 ng g<sup>-1</sup> lipid weight as compared to 540 ng g<sup>-1</sup> in 1985.

**Conclusion:** Levels of POPs contamination in Israel measured in breast milk have declined significantly. Israel ranks among the lowest for POPs exposure levels in OECD countries.



## Maternal Prenatal Smoking and Hearing Loss Among Adolescents

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**Background:** The possible association between prenatal smoke exposure and sensorineural hearing loss (SNHL) has not been investigated despite the fact that more than 12% of U.S. children currently experience such exposure.

**Method:** Cross-sectional data for 964 adolescents aged 12 to 15 years from the U.S. National Health and Nutrition Examination Survey were examined to investigate whether exposure to prenatal tobacco smoke is independently associated with SNHL in adolescents. Participants underwent standardized audiometric testing, and serum cotinine levels and self-reports were used to identify adolescents exposed to second-hand smoke and active smokers. Prenatal exposure was identified by an affirmative parental response to, “Did [Sample Person’s Name] biological mother smoke at any time while she was pregnant with [him/her]?” SNHL was defined as an average pure-tone hearing level more than 15 dB for 0.5, 1, and 2 kHz (low frequency) and 3, 4, 6, and 8 kHz (high frequency).

**Results:** Maternal smoking while pregnant was reported by 16.2% of parents. In bivariate analyses, prenatal smoke exposure was associated with elevated pure-tone hearing thresholds at 2 and 6 kHz ( $p < 0.05$ ), a higher rate of unilateral low-frequency SNHL (17.6% vs 7.1%;  $p < 0.05$ ), and a 2.6-fold increased risk of unilateral low-frequency SNHL in multivariate analyses (95% CI, 1.1-6.4).

**Conclusions:** Prenatal smoke exposure is independently associated with higher pure-tone hearing thresholds and an almost 3-fold increase in rates of unilateral low-frequency hearing loss among adolescents. This is the first data suggesting that *in utero* exposure to tobacco smoke may be injurious to the auditory system.



## Using Pollutant Release and Transfer Registry Data for Environmental Health Research: A Scoping Review

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**Background:** Pollutant release and transfer registers (PRTRs) collect information on chemicals introduced to the environment, mainly by industry. This data supports the public's right to know and provides useful information that can be used to gauge performance of facilities, sectors and governments. The extent to which this data has been used in research, particularly in relation to human health, has not been documented. Our objectives were to learn the extent and nature of the use of PRTR data in scholarly literature with an emphasis on environmental health.

**Methods:** Broad literature searches (1994-2011) were performed using 11 search engines and various key words. Reviewed articles were selected following predefined criteria and data was extracted and analyzed to form a scoping review.

**Results:** After a broad search, 184 were identified; 40 investigated possible relations with health outcomes. Of these, 25 investigated relationships with cancer and 32 identified positive associations between pollutants and health outcomes. One hundred seventy-two explored other uses of PRTR data. Several papers identified challenges, some imputable to the PRTR data, that may contribute to the low number of papers identified.

**Conclusion:** PRTR data is useful for research, including health-related studies, and has significant potential to influence public policy, environmental management practices and ultimately, human health. Although PRTR data has limitations, it is still a unique and useful information source that has not been fully exploited. Developing strategies to overcome limitations could improve data quality and increase its utility in future environmental health research and policy applications.



## Nonanthropogenic Dust Exposure and Asthma Symptoms in Children

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**Background:** Studies have shown a positive association between air pollutants and asthma in children. The Negev desert in Israel is frequently subjected to dust storms (DS) originating from arid soils. The evidence regarding the association with non anthropogenic particulate matter (PM) due to DS is limited.

**Methods:** In order to assess the impact of DS on asthma/wheezing hospitalizations and asthma medications utilization, we identified 42,920 children with asthma, wheezing or asthma-like symptoms, of whom 2,418 were hospitalized in Soroka University Medical Center during 2005-2011. Meteorological and air pollution data were obtained. An air polluted day was defined as a day with a PM10 concentration 2 standard deviations above the background. We used generalized additive models for time series analysis that adjusted the DS effect to seasonality, temperature, relative humidity and day of the week.

**Results:** The majority of children were males (53.8%), 50% were under 2 years of age and 59.6% were Bedouin-Arabs. The number of DS days was 289 (12%). DS increased the risk for the same-day hospitalization and medication dispensing by 1.11 (95%CI 0.95-1.28,  $P=0.05$ ) and 1.05 (95% CI 0.99-1.11,  $P=0.06$ ), respectively. Exclusion of children with respiratory infections did not change the inference. In summer, the association of DS with medications was positive and statistically significant on the third day following DS (RR =1.22, 95%CI 0.80-1.38,  $P<0.01$ ). The positive significant effect of DS was shown only among Bedouin-Arabs, both with hospitalizations and dispensing (RR=1.27, 95%CI 1.10-1.45,  $P<0.01$ ; RR=1.06 95% CI 1.00-1.12,  $P=0.03$ , respectively), reflecting higher susceptibility of this group to outdoor PM fluctuations. Medication purchases may serve as an indicator of mild exacerbations of asthma.

**Conclusion:** The high PM10 levels during DS days increase the risk for asthma hospitalizations and need for asthma medications among children. Bedouin children are at greater risk, partially due to residing in temporary dwelling conditions.