

## **Environmental chemical hazards and child health**

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### **Abstract**

**Objectives:** To review the recent medical literature on environmental chemical hazards to child health.

**Sources of data:** Articles published on this subject between 1999 and 2005 were searched in the MEDLINE database. Books, manuals and statements on child environmental health, issued by institutions such as the American Academy of Pediatrics and the World Health Organization, were also reviewed.

**Summary of the findings:** There has been a growing concern in the last few years with the exposure of children to environmental chemicals. Around 85,000 synthetic chemicals are produced today, and 2,800 of them are mass-produced. There is little knowledge regarding their effects on developing organisms. Children have a greater exposure to environmental pollutants than adults, because their metabolic needs and behaviors (e.g.: crawling, bringing objects to the mouth, playing closer to the ground) put them at special risk of contact with chemicals when they breathe, eat, drink or play. Heavy metals, pesticides, persistent organic pollutants and, at home, environmental tobacco smoke have been associated with the increasing number of diseases such as asthma, neurodevelopmental disorders and childhood cancer.

**Conclusion:** Screening of risk situations using tools such as Environmental History has been stimulated alongside a greater commitment of pediatricians towards measures that can reduce the exposure of children and adolescents to environmental chemicals.

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### **Introduction**

Environmental conditions are among the major factors that determine children's health. Unfavorable situations regarding access to drinkable water, sewage disposal and housing conditions contribute to remarkable morbidity and mortality of children in developing countries.<sup>1</sup> Moreover, there has been a growing concern all over the world in the last decades with environmental contamination by chemical agents produced by industrial, mining and agricultural activities, and with their possible relationship with the increase in the prevalence of congenital malformations, asthma, cancer, and neurological and behavioral disorders in children in recent years.<sup>2</sup>

Currently, around 85,000 chemical agents are produced and used in industrialized countries, 2,800 of which are mass-produced (over 500,000 kg a year). Less than 45% of these agents have undergone basic toxicological tests and less than 10% have been investigated as to their toxic effects on developing organisms.

Children are especially vulnerable to the exposure to environmental chemical agents, due to their physiological characteristics: they drink more water, eat more, and breathe in a greater amount of air per kg than adults do. An infant up to the sixth month of life drinks seven times more water, while a preschooler (1 to 5 years old) eats three or four times more per body weight than an average adult. Oxygen supply in a resting infant is twice as high as that which is observed in an adult. On top of that, the hand-to-mouth habit and playing or moving close to the ground contribute to children's greater exposure. Thus, any chemical agents found in water, air, soil and foods are more likely to be ingested by children than by adults.<sup>3</sup>

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Due to the paucity of information about the consequences of such an exposure, a new and challenging field of research has been taking shape: environmental health in pediatrics. This field seeks to shed some light on the effects of environmental exposures to chemical or physical (e.g.: ionizing radiation) agents and on how these agents reach the children, and thus seeks to help with the prevention, diagnosis and management of various diseases that are possibly caused or aggravated by these conditions.<sup>4-7</sup>

The aim of the present review is to provide information about the susceptibility of children to the exposure to environmental chemical agents, placing special emphasis on the moments of greater vulnerability from intrauterine life to adolescence. It also describes specific aspects of the agents or groups of agents (heavy metals, pesticides, persistent organic pollutants) of greatest interest in our setting and suggests tools, such as environmental history, which can be useful in finding and applying solutions to the problem.<sup>8,9</sup>

### **Exposure to chemical agents and developmental stages**

The risk of exposure to chemical agents may be present in intrauterine life (fetal growth period). The term placental "barrier" has become completely inadequate after those events involving thalidomide and diethylstilbestrol in the 1950s and 1960s.<sup>10</sup>

Besides drugs, lipophilic chemical contaminants such as polycyclic aromatic hydrocarbons (found in cigarette smoke), organic mercury compounds (methylmercury) and ethyl alcohol can easily cross the placenta.<sup>11</sup>

Some essential processes, such as the central nervous system development, predominantly occur during fetal life and during the first years of life. These processes include differentiation of the cerebral cortex, neuronal migration, synaptogenesis and myelination.<sup>12</sup> Fetal vulnerability and the neurotoxicity of some of the aforementioned agents during this period have been extensively documented in cases of fetal alcohol syndrome and in severe neurological disorders observed in Iraqi children who had been exposed to methylmercury during their intrauterine life due to their mothers' intake of bread contaminated with mercury fungicides in the 1970s.<sup>13</sup> In the neonatal period, there is a higher risk for the uptake of chemical agents through the skin, since keratinization is only complete around the fifth to eighth day of life. In addition, the body surface/mass ratio is greater in newborn infants than in older children and in adults. For a given exposed area, a newborn infant absorbs three times more than, and a child twice as much as, an adult.<sup>11</sup>

The metabolic pathways of chemical agents that enter the body are not fully developed at birth and during the first months of life. The capacity to metabolize, detoxify and excrete many chemical agents is different from that observed in adults. In many cases, as in exposures to lead and organophosphates, children are less able to fight these agents due to the fact that they lack or are deficient in enzymes that could metabolize them and eliminate them.<sup>2</sup>

Another important aspect is that occasional difficulties in metabolizing toxic agents may result in the buildup of these agents in storage organs or tissues (e.g.: bones and adipocytes) in case of continued or chronic exposure of children. Given the life expectancy of these children, the consequences of these exposures may be observed only several years later, for instance, possible development of cancer associated with exposure to cigarette smoke components, from intrauterine life to the household environment during childhood.<sup>14</sup>

Processes caused by biological agents such as bacterial infections or environmental exposure to fungi, or by chemical air pollutants (e.g.: cigarette smoke or products from fuel combustion), certainly interfere with lung development. The proliferation of alveoli and pulmonary capillaries begins in the fetal period and extends to the fifth or eighth years of life, and problems during the normal development of this process may cause permanent sequelae on the morphology and function of the respiratory tract.

Older children (at preschool or school age) interact more constantly with the surrounding environment, due to their nutritional and metabolic requirements, and behavioral characteristics. Besides the household environment, new environments such as leisure areas and school may expose children to chemical contaminants.<sup>15</sup> One should recall that, in the so-called developing countries like Brazil, many children live, go to school, and play in places where the soil is highly contaminated by industrial waste, or in areas that are too close to garbage dumps or polluted water sources.

Finally, in adolescents, the quick development of the endocrine system towards sexual maturity is a vulnerable target, making them susceptible to related disorders.<sup>5</sup> Entry into the job market, which sometimes involves activities that are unhealthy and inappropriate for children and adolescents, becomes a possible risk of exposure to toxic substances.

### ***Chemical agents of interest in our setting***

#### *Lead*

The effects produced by the exposure of children to lead have been well documented for over 100 years.<sup>14</sup> With the improved knowledge about the possible effects of lead on child development, blood lead levels currently tolerated are five times lower than those accepted in the 1970s.

The fact that apparently asymptomatic children had low IQ scores, difficulty expressing themselves verbally, attention disorders and behavioral problems was crucial for the establishment of increasingly lower acceptable levels.

The mechanisms through which lead affects the central nervous system functions remain unclear, but its interference in calcium transport and possible effect on the development and maturation of neuronal connections may lie in the genesis of the observed involvement.<sup>14</sup>

In addition to the central nervous system, the urinary tract (kidneys) and the biosynthesis of hemoglobin are the other targets of toxic lead action, and anemia is a common finding in this type of exposure.

Lead pollution persists on a worldwide basis due to its use in metallurgy, manufacture of car batteries, ammunition industries, manufacture of crystals and production of paints and dyes. Organic compounds (tetraethyl lead) are no longer used as fuel additives in Brazil, but they are still used as such in other Mercosur countries.

Acute lead toxicity is rarely described in children nowadays, and is characterized by severe CNS involvement (encephalopathy), which may develop into seizures followed by coma and death if appropriate life support and specific treatment with chelating agents (e.g.: dimercaprol and edetate calcium disodium) are not available.

### *Mercury*

Mercury is one of the most abundant metals on Earth. In addition to natural sources, it is found in various human activities, such as mineral extraction, coal combustion (thermoelectric plants), electronic industry, paper industry, and pulp bleaching (where mercury is used in the electrolytic process for the procurement of chlorine, being one of the resultant residues).

Metallic mercury, discharged into rivers and oceans, enters the food chain and turns into an organic compound (methylmercury) and is then submitted to biomagnification, where growing concentrations are observed even at the top of the food chain, which comprises large predator fish, which are eventually eaten by humans. Organic mercury compounds are highly absorbed via food intake, opposed to metallic mercury, whose uptake is negligible.

Just like lead, organic mercury is toxic to the developing brain.<sup>13</sup> Studies with children exposed to methylmercury *in utero* showed adverse effects on intelligence and poor performance in speech, attention and memory.

Exposures to high levels of mercury, as the ones that occurred in Minamata Bay and in Iraq, cause cerebral palsy and remarkable mental retardation.<sup>16</sup>

More recent studies, conducted in the Seychelles, Indian ocean and on the Faroe islands in the North Atlantic, which included children whose mothers had eaten contaminated fish during pregnancy, have yielded controversial results. Whereas in the former one there was no correlation between the levels of mercury detected in mothers and the cognitive development of concepti, there was an association between mercury levels detected at birth in umbilical cord blood (mean of 22.9 micrograms/liter) and poor cognitive performance at eight years of life in the second study.<sup>13</sup>

In Brazil, the possible effects of the extensive use of mercury in gold mining in the Amazon Basin still have to be evaluated.

### *Pesticides*

Pesticides for agricultural or domestic use, besides their significant morbidity and mortality from acute exposure, especially in developing countries, are a concern in terms of their long-term effects on the health of children exposed through water and soil contamination and food residues.

Organochlorine pesticides (DDT, hexachlorobenzene, aldrin) have a large environmental persistence and, although they were taken out of the market many years ago or been used sparingly nowadays, they can be found in farmlands or in industrial areas where they had been produced. Lactating women can mobilize organochlorine residuals from body stores (fat) and incorporate them into breastmilk. Animal studies have demonstrated the relationship of these agents with carcinogenesis, teratogenesis, immunotoxic effects and as endocrine disrupters.<sup>17</sup>

Organophosphate pesticides, such as malathion, chlorpyrifos, diazinon, and carbamates (e.g.: carbaryl) are widely used all over the world for pest control. Their mechanism of action is related to acetylcholinesterase inhibition. The essential role of acetylcholinesterase in the developmental stage (modeling) of neuronal connections in the central nervous system seems to be well established. Therefore, one cannot rule out the possibility that children who are continuously exposed to these agents may develop some problems, with possible neurobehavioral disorders as a result.<sup>14</sup>

### *Persistent organic pollutants (POPs)*

Besides organochlorine pesticides, other compounds that are environmentally persistent and build up in storage tissues (e.g.: adipose tissue) have been investigated as to their toxicity to developing organisms. Among these compounds we have polychlorinated biphenyls (PCBs) and the dioxin group, whose best known member is tetrachloro-dibenzodioxin (TCDD). PCBs used to be employed because they made excellent electric and thermal insulating materials, especially for electrical transformers. Although their use was banned, they are still found in the environment due to industrial residues with occasional water and food contamination.

Dioxins may be present in chlorophenoxy (2-4-dichlorophenoxyacetic acid) herbicides, nowadays in lesser amounts than in the past, but mainly as a by-product of the combustion of materials containing chlorine, as occurs in the incineration of industrial waste or garbage.<sup>13</sup>

PCBs and dioxins have been associated in animals studies with carcinogenesis and with the role of endocrine disrupters, with consequences such as low sperm count and infertility.<sup>17</sup>

### *Tobacco smoke*

Tobacco smoke contains a wide range of chemical agents, including carbon monoxide and sulfur dioxide (also found in air pollution emissions in big cities, either from motor vehicles or industrial activities), and extremely toxic compounds, such as hydrogen cyanide, and carcinogenic substances (e.g.: benzopyrene).

The harmful effects of passive exposure of children to cigarette smoke and correlates can be felt *in utero*, extending throughout childhood. The effects of smoking on pregnancy include miscarriage, low birth weight and cognitive disorders. The association of tobacco smoke

exposure in the household with recurrent otitis, lower airway infections, and induction or exacerbation of bronchial asthma<sup>14</sup> in children has been well documented. There also seems to be an association between the incidence of cancer in adulthood and exposure to tobacco smoke in childhood.<sup>14</sup>

### **Environmental exposure to chemical agents and childhood diseases**

There seems to be a great amount of information and evidence, some of which is based on consistent epidemiological studies, that the occurrence of some diseases or group of diseases has increased in the last decades, especially in northern hemisphere countries.<sup>2,14,16</sup>

This trend has also been observed in industrialized regions and in big cities in developing countries.

Among the several factors that could explain this increase are the improvement in diagnostic tools (as in the case of childhood cancer), greater exposure to chemical agents (e.g.: air pollutants and pesticides), and to physical agents (e.g.: electromagnetic radiation).

### **Asthma**

Asthma incidence among children aged less than 18 years increased more than twice in the United States<sup>2</sup> and in other industrialized countries in the last decade. The major triggers of acute asthma attacks are cigarette smoke (at home), volatile organic compounds found in construction materials, cleaning products, adhesives, and pesticides. In the external environment of big cities, ozone (O<sub>3</sub>) and sulfur dioxide (SO<sub>2</sub>), produced by motor vehicles or by industries and thermoelectric plants, together with particulate material, have a key role in the development of asthma attacks. These chemical agents add up to external biological factors (allergens), such as pollen, fungi, dust mites and others, affecting mainly those children who live under poor housing conditions.<sup>14</sup>

### **Cancer**

Despite the reduction in mortality rates and an increase in survival rates, due to diagnostic improvements and anticancer treatments in recent years, the incidence of some types of childhood cancer has surprisingly risen. The incidence of acute lymphoblastic leukemia increased nearly 30% between the 1970s and the 1990s in the United States, rising from 2.8 cases per every 100,000 children to 3.5: 100,000.<sup>2</sup> Between 1973 and 1994, the incidence of brain cancer increased by 39.6%, with a similar behavior between males and females.<sup>3</sup> Other types of cancer, found in young adults who had just grown out of adolescence, such as testicular cancer, increased by 68 % in the same time period.<sup>2</sup>

A question that is still open is whether the improvements in diagnosis and case notification could explain such increases or whether the presence of chemical agents in the environment, given the high geographical correlation found

in some cases, might be related to the collected epidemiological data.<sup>18</sup>

### **Neurological developmental disorders**

It has been estimated that around 6% of live births in the United States may have neurobehavioral disorders, from attention deficit/hyperactivity disorder to autism. The causes have not been clearly established yet, but the association of agents, such as heavy metals (lead, mercury), certain pesticides and persistent organic pollutants (polychlorinated biphenyls) with brain injury in children is widely known, as previously described. Neurological developmental disorders probably result from the interaction between environmental factors and the individual susceptibility of every child, such as genetic predisposition. However, there is no doubt that exposures to high concentrations of agents such as organic mercurials, under certain circumstances (*in utero*), may, in isolation, cause remarkable damage.<sup>17</sup>

### **Endocrine disruption**

Endocrine disrupters are natural or exogenous synthetic chemical agents that can mimic or modify the action of hormones.<sup>14</sup> Initially, the term was used to describe agents with estrogenic effects, such as estrogens found in plants and in foods of vegetable origin. Currently, the term is also used for disrupters of thyroid function or pancreatic islets (insulin producers) or for those which modify androgenic activity.

Even though few studies have been conducted with humans, some organic chlorinated compounds, such as DDT and chlordecone and polychlorinated biphenyls, revealed estrogenic activity in laboratory studies. Reproductive and fertility disorders were investigated in wild animals, such as birds and reptiles.

In human beings, an association has been made between exposure to endocrine disrupters and the increase in the incidence of hypospadias in boys and the increasingly earlier onset of puberty in girls.<sup>2</sup>

### **Environmental history in pediatrics**

Currently, the training of health professionals and pediatricians does not include environmental health studies, which would properly prepare them for the recognition, treatment and prevention of environmentally related diseases and exposures. Due to biological, psychological, behavioral and social discrepancies between adults and children, there is the necessity for specific education of pediatricians in pediatric environmental health by including such syllabus in the School of Medicine curriculum, in Medical Residency programs and in continued education.<sup>19</sup>

The World Health Organization acknowledges that it is necessary to educate and train health professionals for the prevention, diagnosis and treatment of diseases related to environmental risk factors, since these diseases are regarded as an important global public health problem. A series of training courses organized by the WHO have been developed,

including the elaboration of teaching materials, information brochures for health professionals and, mainly, the promotion of Environmental History in Pediatrics as an integrating part of standard medical History.<sup>20,21</sup>

One of the roles of a pediatrician is to guide and instruct parents and family members on how to reduce or prevent exposures to the most common and potentially harmful chemical substances, but special attention should also be paid to new risks and to the effects produced by prolonged low-dose exposure (chronic exposure).<sup>22,23</sup> Many of the currently described and well-documented environmental risks were first discovered by the observation and investigation of some clinicians, for instance, the neurological disorders caused by methylmercury in Minamata, the congenital malformations caused by ethyl alcohol, among others.<sup>24</sup>

A survey conducted by Kilpatrick et al. with pediatricians in Georgia (USA) about their knowledge of Environmental History revealed that only one in five pediatricians had had a training course in this area, but all of them believed that the information obtained through History could detect harmful exposures.<sup>25</sup>

Observing the incidence and prevalence of diseases and using such information for interventions is a well-established strategy used in Public Health approaches; the necessity to follow up chronic diseases mediated by environmental factors in children has been increasingly acknowledged. It is believed that at least three clinical situations, as previously described, are correlated or may be exacerbated by the exposure to certain environmental agents: asthma, cancer and neurological development disorders.<sup>16</sup>

Information about the environment is important for children's health and should be included in every complete pediatric history.<sup>14,26</sup>

What is environmental history in Pediatrics? It is a series of basic and concise questions that allow pediatricians to identify possible exposures of children to several chemical, physical and biological environmental factors, according to their specific vulnerabilities at each developmental stage. These questions reflect the regional social aspects of each population, and it is important that environmental history be carried out on a routine basis with all children (symptomatic or not).<sup>14,10,27,28</sup>

Environmental history, together with clinical history, allows health professionals to keep track of external and internal environmental conditions, behaviors and risk factors that are important to children's health. Examples include characteristics of the house, school, day care centers and recreation areas; proximity to garbage dumps; urban regions with heavy traffic and with polluting industries; potential exposure to pesticides or other chemical products, among others.<sup>29</sup>

Nowadays, there are specialized units that keep track of diseases and other problems related to environmental factors in the USA, Canada, Mexico and Spain, as well as other initiatives in Argentina and Uruguay. Since most health professionals do not have enough knowledge about the effects caused by exposures to chemical and physical

agents, these specialized units play a crucial role in the diagnosis and follow-up of patients, provision of information to the population, research, training of health professionals and implementation of preventive measures.<sup>30</sup>

### **Investigation of environmental risks**

Some questions have been suggested for investigating the risks posed by the household environment, and may be used as a guideline for the appointment with a pediatrician or as a questionnaire to be filled out by the parents.<sup>14</sup>

The information obtained from this questionnaire can lead to specific investigation of the environment and the child, parent counseling for the elimination of possible risks and recommendation of preventive measures. One should recall that the investigation has to include all the places children go to or spend most of their time in (e.g.: day care center, school, houses of other family members), taking their age into account. The regional and sociocultural characteristics should also be carefully observed while evaluating the environment where children live.

### ***Where does the child live, play and/or go to school?***

*Is it an urban or rural area?*

How close is the house to industries, crop fields, polluted rivers or areas?

What is the source of water supply (treated water, well water, etc)

Are sanitation and garbage collection available?

What is the general state of the house?

How many people live in the house? How many rooms are there?

What are the general ventilation and temperature conditions of the household environment?

Is the house being restored?

Are there any leaks and/or moldy walls?

What kind of fuel is used for cooking and heating of the house or of the water (gas, kerosene, wood, coal)?

What kinds of cleaning products and air fresheners are used?

What kinds of insecticides and pesticides are used in the house and in surrounding areas?

Where does the child play?

Are there any smokers in the house?

### *Hobbies*

What types of hobbies do the children and other household members have?

What substances are used in the household? (solvents, paints, glues, etc.)

### *Work-related exposures*

What professions or activities are household members engaged in?

Do their professional activities involve potentially hazardous substances, such as pesticides, metals, fibers, solvents, among others?

Does any family member work at home?

Does the child or adolescent do any kind of work? If so, describe it.

### **Conclusions: the role of pediatricians in environmental health promotion**

As we may perceive, pediatricians and other health professionals who treat children and adolescents are entrusted with the task of recognizing the hazards that environmental chemical agents may pose. This task should not be limited to developing skills for the detection of already established health damage or for the implementation of proper preventive measures in the environment shared by children. It is high time pediatricians, along with other professionals, organizations such as environmental organizations, centers for information and toxicological assistance, and non-governmental organizations for the protection of children and of the environment, actively struggle for legislative measures that properly protect our children and adolescents from environmental contamination by chemical agents.<sup>9,30</sup>

Pediatricians may help promote better environmental health among their patients and in the community where they work in different ways. The inclusion of related topics in usual guidelines (e.g.: vaccination schemes) would be an important step. Measures such as sorting out and recycling garbage, using less pesticide in the household environment, and encouraging the intake of natural foods instead of industrialized ones are some examples of habits that should be promoted.<sup>17,31</sup> In the community, participation in campaigns for less polluting alternative sources of energy (wind power, solar energy) and for reduced circulation of motor vehicles (good-quality public transportation and implementation of bicycle paths) may contribute to the improvement of environmental conditions in urban centers. Strategies for the preservation of water sources and forests are trends that should be supported by everybody.<sup>17</sup> Finally, at the regional and national levels, pediatricians should engage in and actively advocate health and legal measures that allow the early detection of environmentally related diseases in children and the availability of resources for their management and prevention.<sup>14,17,31</sup>

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