

ENVIRONMENTAL EXPOSURE AND BIRTH OUTCOMES

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Abstract

The influence of environmental hazards on the health of children is one of the major current concerns in environmental health. Scientific investigations are now focusing on identifying and understanding the role of environmental hazards in the development of birth outcomes that result from in utero exposure to environmental contaminants.

This paper reviews the published literature with provided evidence concerning the impact of environmental exposures to chemicals on the incidence of birth outcomes in the areas of environmental pollution originating from various sources. In spite of methodological limitations in a number of reviewed studies, the present body of knowledge calls for a precautionary approach and for preventive measures in order to reduce the risk of environmental exposures to chemicals with a recognized or suspected potential to cause birth outcomes.

Key words:

Birth outcomes, Environmental health hazards, Environmental exposure

INTRODUCTION

One of the topical research concerns related to the impact of the environment on human health is the influence of environmental hazards on the child's health and development. The conference of European ministers of health and of the environment, organized by the World Health Organization (WHO) in London in 1999 adopted a resolution according to which the child's health care in the environment was acknowledged a priority in the environmental protection policy and in research issues. This priority was extended to a global scale at the conference of WHO member states in Kuala Lumpur in 2002.

Birth defects are the leading cause of infant mortality in the developed countries. Although according to various indicators (e.g., infant mortality) children's health has

been improving, the rates of birth defects have not followed the same pace. In the USA, the proportion of infant mortality due to birth defects increased from 14% in 1968 to 22% in 1997 [1].

The causes of most birth defects remain unknown, but the growing literature indicates that environmental factors may cause genetic mutations and interact with genetic factors predisposing to birth defects [2]. Such scientific findings are of significant importance for the public health policy and practice as they highlight that birth defects may be largely preventable.

This paper is a concise review of the literature, discussing the evidence that environmental factors may contribute to the development of birth outcomes.

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CONTRIBUTION OF ENVIRONMENTAL POLLUTANTS TO THE ETIOLOGY OF BIRTH OUTCOMES

Based on the current knowledge, the etiology of about 40% of birth defects has been recognized to date. Among various birth defects of known etiology, approx. 36% are caused exclusively by genetic factors, whereas 50–75% result from complex gen-environmental interactions [2,3]. According to the studies carried out by Brent and Beckman [4], 10% of major types of congenital malformations are attributed to substances of proved teratogenic effects, while 37% to interactions of genetic and environmental factors.

So far, about 2500 substances have been recognized as teratogenic agents, 40 of them (e.g., carbon monoxide, ozone, lead chromate, lead acetate, lead phosphate, 1,2-dibromo-3-chloropropane, 2-bromopropane) are proven to induce teratogenic effects in humans [5].

Examples of environmental factors associated with low birth weight, preterm births and birth defects are presented in Table 1 [2].

Numerous studies investigating the etiology of birth defects and developmental disabilities indicate that environmental pollutants may significantly affect the prevalence of birth outcomes.

Shaw et al. [6] indicated that children from mothers, who during pregnancy lived near potential sources of environmental pollution, i.e. industrial plants, waste landfills, hazardous materials storage sites or wastewater discharge sites, were at higher risk of the heart and circulatory system malformations (OR = 1.5; 95%CI: 1.1–2.0). Based on the analysis of the impact of various groups of chemicals, the authors found that the increased risk applied only to children from mothers exposed to heavy metals (OR = 1.5; 95%CI: 1.1–2.3) and cyanides (OR = 2.2; 95%CI: 1.3–3.9). Similarly, Vinceti et al. [7] demonstrated excess risk of cardiovascular defects, oral clefts and musculoskeletal anomalies in the lead polluted area of northern Italy.

Birth defects have been repeatedly reported to be associated with several common paternal occupations [8].

Literature confirms a significant correlation between congenital malformations and developmental defects in chil-

Table 1. Environmental factors associated with low birth weight (1), preterm births (2), and birth defects (3) in human epidemiological studies [2]

Agent/Exposure	1	2	3
Toxic substances:			
electronics assembly	X		
hair dye			X
lead	X	X	X
polychlorinated biphenyls	X		X
soldering			X
solvents	X		X
paint			X
benzene	X		X
carbon tetrachloride	X		X
toluene	X		X
tetrachloroethylene			X
trichloroethylene			X
styrene monomer	X		
Pesticides:			
agricultural work	X		X
Pollutants:			
carbon monoxide	X		X
trihalomethanes	X		X
hazardous waste	X	X	X
methylmercury			X
particulate matter	X		
Physical:			
high altitude	X		
ionizing radiation	X	X	X
noise	X		
work stress	X		

dren born to mothers exposed to mercury during pregnancy [9]. Reports by the National Research Council (NCR) indicate that over 60 000 children born annually in the United States may develop nervous system disabilities, resulting from exposure to mercury in food of their mothers.

AIR POLLUTION

Number of published studies demonstrate that outdoor and indoor air pollutants may increase the risk of birth defects and other adverse birth outcomes, including low birth weight and intrauterine growth retardation.

Jędrychowski et al. [10] surveyed pregnant women in Poland exposed to fine particulate matter ($PM_{2.5}$) and assessed its effects on birth outcomes. The newborns from mothers exposed to higher concentrations of fine particles (above the median of $36.3 \mu g/m^3$) showed significantly shorter body length at birth, lower birth weight and reduced head circumference. Predicted reduction in birth weight at an increase in exposure from 10 to $50 \mu g/m^3$ was 140.3 g and the corresponding predicted reductions of the body length and head circumference would be 1.0 cm and 0.5 cm, respectively.

The study carried out by Ritz et al. [11] in south California, USA, demonstrated a statistically significant correlation between the air pollution and the risk of birth defects in those children whose mothers lived in the area with an increased content of carbon monoxide, nitrogen dioxide, ozone and suspended dust ($PM < 10 \mu$) in the air. The results obtained by the authors point to an increased risk of cardiac ventricular septal defects in children whose mothers in the second (OR = 1.62; 95%CI: 1.05–2.48), third (OR = 2.09; 95%CI: 1.19–3.67) and fourth (OR = 2.95; 95%CI: 1.44–6.05) month of pregnancy were exposed to carbon monoxide in the air. Similarly, the risk of defects of aortic artery and valve, pulmonary artery and valve anomalies, and conotruncal defects increases in children whose mothers were exposed to the increased air concentration of ozone (1.07–2.86 ppm) during the second month of pregnancy.

Low birth weight and intrauterine growth retardation in progeny may also be associated with mothers' exposure to sulfur dioxide, nitrogen oxides and dust suspended in the air in the first trimester of pregnancy [12–14].

Air pollution may cause DNA impairments and disturb its transcription. The presence of trichloroethylene and toluene in the air may cause some developmental defects in children, such as so called Fetal Toluene Syndrome, similar to the developmental defects associated with the consumption of alcohol during pregnancy [15,16].

CONTAMINATED FOOD AND DRINKING WATER

Incidents known as “Minamata”, “Yusho”, and “Yu-Cheng” diseases, in Japan and Taiwan, are examples of birth de-

fects, which resulted from consumption of contaminated food. In the first case, fish, a major component of the local diet, has become contaminated with methyl mercury as the result of industrial discharges of mercury into Minamata Bay. Consumption of the contaminated fish led to the outbreak of developmental disabilities, including microcephaly, cerebral palsy, cleft lip and palate. Yusho and Yu-Cheng diseases were caused by consumption of food contaminated with polychlorinated biphenyls (PCBs) in result of two accidents in Japan and Taiwan, respectively. The poisoning led among others to low birth weight and multiple deformations in newborns from exposed mothers [17].

Drinking water, contaminated with products formed in the process of water chlorination (trihalomethanes, haloacetic acids, chlorophenols, chloral hydrate, haloacetonitriles), constitutes one of the major environmental hazards contributing to the congenital malformations and developmental disabilities in children [18].

Hwang et al. [19] in a Norwegian cross-sectional study of 285 631 births during 1993–1998 indicated an increased risk of birth defects (OR = 1.13; 95%CI: 1.01–1.25), including circulatory defects (OR = 1.37; 95%CI: 1.00–1.89), urinary tract defects (OR = 1.46; 95%CI: 1.00–2.13), and neural tube defects (OR = 2.60; 95%CI: 1.30–5.26) due to exposure to chlorination by-products (trihalomethanes) present in tap water. An analysis of the risk of particular types of birth defects showed that the magnitude of the risk of ventricular septal defects depended on the level of water chlorination: OR = 1.63; 95%CI: 1.02–2.58 and OR = 1.81; 95%CI: 1.05–3.09 for medium and high levels, respectively. Based on the analysis of 1893 live births and assessment of their correlation with the data on drinking water quality, Gallagher et al. [20] demonstrated an increased risk of low birth weights in children whose mothers consumed drinking water contaminated with trihalomethanes during the first trimester of pregnancy (OR = 5.9; 95%CI: 2.0–17.0). Another study of 141 077 children born during 1993–1995 in Norway, whose mothers consumed chlorinated drinking water, confirmed an increased risk of birth defects, i.e. urinary tract defects (OR = 1.99; 95%CI: 1.10–3.57), resulting from exposure to products arising from drinking water chlorination [21].

The case-control study covering 112 cases of neural tube defects in a group of children born during 1993–1994 in New Jersey, USA, showed a statistically significant correlation (OR = 2.1; 95%CI: 1.1–4.0) with mothers' exposure at pregnancy to trihalomethanes by the consumption of chlorinated drinking water [22].

Croen et al. [23] in a case-control study of 538 children born with neural tube defects and 539 births without any defect demonstrated that mothers' exposure to nitrates present in drinking water at a concentration above 5 mg/l leads to an increased risk of anencephaly in newborns (OR = 6.9; 95%CI: 1.9–24.9 for 36–67 mg/l).

Hwang et al. [24] concluded that their meta-analysis provide evidence that exposure to water chlorination products increases the risk of any birth defect, including neural tube and urinary system defects. The results for the respiratory system, major cardiac and oral cleft defects were heterogeneous and inconclusive.

PESTICIDES

Epidemiological studies carried out worldwide show correlations between parents' environmental and occupational exposure to pesticides and congenital malformations and developmental disabilities in progeny, e.g., heart deformities and cardiovascular defects, central nervous system and musculoskeletal defects, oral clefts, spina bifida, anencephaly, and limb reduction [25].

Garcia et al. [26] in a case-control study, carried out in Spain, found that the risk of birth defects, such as nervous system defects, oral clefts, and multiple other anomalies was three times higher in children whose mothers were occupationally exposed to pesticides in the first trimester of pregnancy (OR = 3.16; 95%CI: 1.11–9.01).

In a case-control study (the Baltimore-Washington Infant Study) covering 4390 cases of heart defects in children born during 1981–1989, Loffredo et al. [27] indicated that the risk of the transposition of the great arteries (OR = 2.8; 95%CI: 1.3–7.2) was over two times higher in children born to mothers exposed to herbicides during the first trimester of pregnancy and over four times higher (OR = 4.7; 95%CI: 1.4–12.1) in children from mothers exposed to rodenticides.

A statistically significant correlation between the parents' exposure to pesticides and biocides (chlorophenoxy herbicide/fungicide) and children's developmental, (circulatory/respiratory, urogenital, and musculoskeletal/integumental) defects was confirmed by Garry et al. [28] in a study covering 4935 births in the population of 34 772 farmers residing in the agricultural part of Minnesota, USA, during 1989–1992. The birth defects occurred almost three times more frequently in the exposed group of farmers compared to the control group, i.e. parents who were not exposed to pesticides ($p < 0.05$).

A study carried out in Finland [29] demonstrated an increased risk of orofacial clefts, nervous system and skeletal defects in children whose mothers were occupationally exposed to pesticides during the first trimester of pregnancy compared to those children whose mothers had no contact with pesticides (OR = 1.4; 95%CI: 0.9–2.0).

The study comprising assessment of contamination of 856 municipal drinking water intakes by pesticides (triazine herbicides) in Iowa, USA, demonstrated an increased relative risk of intrauterine growth retardation in children (RR = 1.8; 95%CI: 1.3–2.7) whose mothers resided in the southern part of the state, characterized by a considerable concentration of the herbicides alachlor, atrazine, metolachlor, 2,4-D and cyanazine in drinking water [30].

HAZARDOUS WASTES

Hazardous waste landfills form a significant source of the release of toxic substances into the environment, including substances causing birth defects in children born to mothers residing during the pregnancy in the vicinity of waste sites.

A number of epidemiological studies, investigating potential links between exposure to toxic substances released from accumulated wastes and health effects in the population residing in the area affected by waste landfills have been conducted in the United States [31–36].

Based on the results of the performed studies, the Agency for Toxic Substances and Disease Register (ATSDR) [37] distinguished 7 major groups of health effects in the population living near various landfills of hazardous wastes.

They comprise cancer, immune system disorders, kidney and liver disorders, diseases of lungs and respiratory system, neurological disorders, and also birth defects and low birth weight.

In particular, low birth weight in children, whose mothers lived near hazardous waste sites during the pregnancy, have been most frequently reported to result from exposure to toxic substances released from the accumulated wastes [31,37–41].

Vianna and Polan [38] indicated that in the population living in the area contaminated with chemicals released from the hazardous Love Canal waste landfill, New York state, USA, over 40% of children, born during the landfill operation in 1950, were characterized by a low birth weight (<2500 g). Similar results were obtained by Goldman et al. [39].

Berry and Bove [40] carried out a retrospective study of 8932 birth certificates and found a statistically significant correlation between the children's low birth weight and mothers' living, during pregnancy, near the Lipari waste landfill, New Jersey, USA.

Industrial hazardous wastes containing toxic substances, mainly chromium, cadmium, lead, nickel, arsenic, benzene, toluene, 1,2-dichloroethane, formaldehyde and phenol, were being discharged on that landfill for 13 years (1958–1971). An analysis of birth certificates issued during three time intervals of the operation of the landfill, corresponding to the attributed extent of the potential exposure to toxic substances released from the accumulated wastes showed: (i) no exposure or insignificant level of exposure related to the initial period of the landfill operation (1961–1965); (ii) medium level of exposure related to the intense use of the landfill (1966–1970); (iii) the highest exposure level resulting from the release of chemical contaminants to the air, soil, ground and surface water (1971–1975); and (iv) no exposure or only slight exposure after remediation of the waste site (1981–1985). According to the results of the study, the lowest average birth weight was noted in children whose mothers lived during pregnancy up to 1 km from the landfill during the highest emission of chemicals from the accumulated wastes (1971–1975) compared to the average birth weight of the children born in the other

time intervals included in the study. The relative risk of the delivery of a child with low birth weight was statistically significantly higher in the exposed group of mothers than in the control group (OR = 5.1; 95%CI: 2.1–12.3).

Kharrazi et al. [41] in a retrospective study of 25 216 births registered in the area within a radius of 5 km from the hazardous waste landfill in California, USA, indicated that the children whose mothers, during pregnancy, lived in the zone of the highest exposure, i.e. at a distance of approx. 1 km from the landfill, were characterized by a significantly lower birth weight (-35.2 g, $p < 0.02$) compared to the children whose mothers resided in a relatively lower exposure zone, i.e. within a radius of 1 to 5 km from the landfill.

However, no statistically significant correlation was found between the children's low birth weight and the distance of mother's residence during pregnancy in the landfill area in another case-control study [42].

Lagakos et al. [43] demonstrated a statistically significant correlation between the consumption of water contaminated with heavy metals and other toxic substances released from the hazardous Woburn waste sites, Massachusetts, USA, and the increased incidence of developmental defects of the central nervous system, eyes and ears, chromosome impairments and oral clefts in the population living in the area affected by the waste landfill.

An increased risk of birth defects in populations living at a distance up to 1.5 km from the waste landfills was demonstrated by Geschwind et al. [44] in a study of 590 hazardous waste sites in New York state. The study involved 9313 children with congenital malformations and over 17 000 healthy children as a control group. The study resulted in the following findings: mothers' living at a distance up to 1.5 km from the investigated sites resulted in a 12% increase in the risk of birth defects in children and a 63% increase in the risk of birth defects was associated with residing near those landfills, which posed the highest ecological hazards. An analysis based on the type of chemicals released from the accumulated wastes indicated the increased risk of the skeletal system defects by 20% in case of exposure to chemical substances released from pesticides, of the nervous system disabilities by 34% in case of exposure to heavy metals, and by 24% in case of

exposure to solvents; and finally of chromosome impairments in newborns by 46% due to exposure to substances released from plastics.

In a study of selected birth defects in the populations living in the vicinity of 764 inactive landfills of hazardous wastes containing heavy metals, solvents and pesticides, Croen et al. [45] observed an increased rate of cardiac disabilities (OR = 4.2; 95%CI: 0.7–26.5) and spina bifida (OR = 2.1; 95%CI: 0.6–7.6) in children whose parents lived at a distance up to 0.5 km from the investigated waste sites, but this increase was not statistically significant.

Similar studies have been conducted in Europe, and the EUROHAZCON international study can serve as an example [46]. The study concerned 21 hazardous waste landfills located in Belgium, Denmark, France, Italy and the UK. The study was based on the birth defects registers in participating countries and included 1089 cases of live healthy newborns, and 2366 cases with birth defects, whose mothers, during pregnancy, lived within a radius of up to 7 km from the hazardous waste landfills. Each study applied a surrogate index of exposure, assuming a 3 km distance of the residence place from the landfill as the potentially highest level of exposure to toxic substances released from the waste sites. The results obtained in respective countries pointed to a reverse dependence of the rate of the birth defects incidence on the distance of the mother's residence from the waste landfill sites.

A relative risk of developmental defects in children whose mothers at pregnancy lived up to 3 km from the waste landfill, amounted jointly to 1.33 (95%CI: 1.11–1.59) for all country projects. An analysis of cases of particular types of birth defects indicated an increased risk of spina bifida (OR = 1.86; 95%CI: 1.24–2.79), malformations of cardiac septa (OR = 1.49; 95%CI: 1.09–2.04) and malformations of great arteries and systemic veins (OR = 1.81; 95%CI: 1.02–3.20). The EUROHAZCON study also indicated the higher incidence of chromosomal aberrations (mothers' age and family's economic status were controlled) in newborns from the areas in the direct vicinity (0–3 km) of 23 hazardous waste landfills, compared to those from further areas (3–7 km) (OR = 1.41; 95%CI: 1.00–1.99) [47].

Studies of relationship between birth defects and specific waste landfill sites [48] and municipal landfills [49] have been carried out in Scotland and in Ireland, respectively. Both studies aimed at assessing relative risks of adverse birth outcomes in populations living near (2–3 km) waste landfills and in those living further away. No statistically significant excess risks of congenital anomalies in populations living in the proximity to waste landfills were found by either of the study.

CONCLUSIONS

The results of the reviewed studies indicate that environmental pollutants may significantly affect the prevalence of birth outcomes. The maternal exposure to pesticides, water chlorination products present in drinking water, accidental food contaminants, chemical substances released from hazardous waste landfills, and some indoor and outdoor ambient air pollutants are associated with the etiology of such birth outcomes as low birth weight, cardiovascular, central nervous system and musculoskeletal defects, oral clefts, spina bifida, anencephaly, limb reduction, and urinary tract defects.

The literature often presents heterogeneous and sometimes inconsistent data on adverse birth outcomes related to environmental exposures. The common difficulty and weakness in the majority of the studies are associated with exposure assessment. Different approaches and inaccurate assessment of exposure, low statistical power and different classification systems are among the main causes of some inconsistencies between individual studies. Nevertheless, current state of knowledge calls for a precautionary approach and preventive measures able to reduce the risk of environmental exposures to chemicals that are known or suspected to cause birth defects and developmental disabilities. Strengthened knowledge and better understanding of the environmental etiology of birth outcomes will help public health policy and practice to develop and implement the sound prevention of exposures and reduction of risks of birth outcomes in newborns.

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