REVIEW

Air pollution and children's health

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ABSTRACT

Air pollution cannot be considered just a regional problem but is a global issue. In the past 70 years billions of tons of carbon dioxide and millions of metric tons of methane, the two key greenhouse gases, have been emitted annually into the atmosphere from production and burning of fossil fuels for energy and transportation. Gases and Particulate Matters have many adverse effects on human health as a consequence of oxidative stress at the cellular level with alteration of the intracellular redox balance stimulating the production of pro inflammatory cytokines and chemokines.

Children are more susceptible to air pollution than adults and the effects of atmospheric pollutant have been demonstrated on the foetus and pre-school child. Ultrafine particles generated by traffic emissions have been suggested to have particularly bad effects on the airways due to high level of pulmonary deposition and their ability to induce inflammation and oxidative stress.

To improve air quality and reduce air pollution the WHO, supported by 109 scientific Societies, Scientific Associations and Patients' Associations, issued new guidelines to reduce atmospheric pollutants in the world. It is important that all pediatricians continue to advocate for measures to protect the foetus and the child from atmospheric pollution as well as treating the consequences.

IMPACT STATEMENT

Air pollution has had a huge increase in the last 70 years. Gases and Particulate Matter directly irritate the airways but can damage all organs of our body carried by the bloodstream. Proactive initiatives are necessary to protect the fetus and child.

KEY WORDS
Air pollution; childrens' health.

INTRODUCTION

From 5 December to 9 December 1952 a heavy smog (dense polluting fog) affected London causing thousands of deaths from respiratory and heart problems. The fog was so thick that people walking the streets could not even see their feet.

When some chemicals mix with water and air, they may be converted into acids which irritate the upper and lower airways and skin, as well as corroding buildings. That winter had been particularly cold with heavy snowfall in the region and people had burned very large quantities of coal in their houses to keep warm (1).

This “heavy fog” was caused by thermal inversion, the causes of which were unknown at the time. Under normal conditions, smoke rises into the atmosphere and is dispersed. However, if an anticyclone forms it pushes the air down, heating it, thus creating a thermal inversion with the air near the ground colder than the air above it. So, when hot smoke comes out of the chimneys it remains trapped at ground level. Furthermore, during the day the sun’s rays are blocked by the thick fog and thus the air at the ground level remains cold. This favors the condensation of water around solid particles creating a thick toxic fog. In the case of London in those days more polluted air had been carried by the winds from the industrial area towards the city further increasing pollution.

The chronicle of the time does not report how many children suffered from this serious pollution, but this and other episodes that occurred previously paved the way for studies on the effects of pollution on the health of the environment and those that live there.

ATMOSPHERIC POLLUTANTS

Worldwide, in the past 70 years, billions of tons of carbon dioxide and more than 120 million metric tons of methane, the two key greenhouse gases, have been emitted annually into the atmosphere from the production and burning of fossil fuels for energy and transportation. The consumption of energy from fossil fuels in 2020 (oil and derivatives, natural gas, and coal) represents 79%, while the energy deriving from non-fossil fuels [nuclear energy, biological fuels, hydroelectric energy, wind energy and other renewable sources] comprises the remaining 21% (2). Among the biofuels, which represent about 3% of this output, part comes from burning wood used in homes for fireplaces.

Atmospheric pollutants are defined as substances present in the air that can harm animals, plants, materials, and humans (**Table 1**) (3)**.**

Primary pollutants include sulfur dioxide, nitrogen oxides (especially nitric oxide and NO2), reactive hydrocarbons [which also include Volatile Organic Compounds (VOCs) present among indoor pollutants, that are not reported in this paper] and carbon monoxide (CO).

Secondary pollutants include ozone (O3) (which is derived from the interaction in the atmosphere between NO2 and hydrocarbons), sulfuric acid which derives from interaction between atmospheric sulfur and ammonium nitrate. This latter is synthesized from atmospheric nitrogen oxides formed in the atmosphere from the primary pollutants.

The corpuscular part of atmospheric pollutants is defined as Particulate Matter (PM) which is named on the basis of the aerodynamic diameter PM-10 (when particles <10 μm in diameter), in PM-2.5 (particles with diameter <2 .5 μm), and the ultra-active particles (UFP) PM-0.1 (diameter <0.1 μm). All PM-2.5 and PM-0.1 are included in PM-10.

All PM are invisible to the naked eye unlike larger particles which are seen as dust under adequate lighting.

The largest PMs can cause ill effects especially in the upper airways, causing coughing and tearing, PM-2.5 easily reach the terminal bronchioles and alveoli and UFPs enter the alveolar capillaries and then systematically to all the cells of the human body where they may cause significant damage (4, 5).

EFFECTS ON HUMAN HEALTH

Air pollution causes almost the same number of deaths worldwide as tobacco smoke (about 7 million a year) and 70% of mortality attributed to non-communicable diseases (6).

The effects of atmospheric pollutants are manifold (**Table 2**):

Immunological: effects on innate and adaptive immunity with inhibition of interferon-gamma synthesis, stimulation of Th2 and Th17 immunity, increased IgE-mediated allergy**,** and eosinophilic inflammation.

On the upper airways: reduction of mucociliary clearance and reduction of antioxidants in the airway lumen.

Cardiovascular: elevation of inflammatory markers and dysregulation of the autonomic system.

Pulmonary: Production of reactive oxygen species (ROS), alteration of phagocytosis.

Table 1. *Air pollutants.*

Primary pollutants:
sulfur dioxide
nitric oxide
nitrogen dioxide
reactive hydrocarbons (including VOCs)
Secondary pollutants:
ozone (O3)
sulfuric acid
Particulate Matter:
PM10
PM2.5
PM2.5

Epigenetics: epigenetic regulation of physiology and susceptibility via DNA methylation, histone acetylation, micro-RNA and other RNA expression, leading to silencing of some genes and expression of other proinflammatory genes (7).

Not all but most of these effects depend on oxidative stress at the cellular level with alteration of the intracellular red-ox balance and stimulation or blockage of nuclear factor erythroid 2–related factor 2 (Nrf2), which is an emerging regulator of cellular resistance to oxidative stress. Nrf2 controls the basal and induced expression of an array of approximately 200 antioxidant response element–dependent genes to regulate the physiological and pathophysiological outcomes of oxidant exposure (8). The basic sequence of events supporting the dynamic redox equilibrium is, therefore, the following: pollutant (or signal); increase in oxidants and/or electrophiles; signal transduction by a redox-sensitive functional shift in the target; feedback activation of a response switching off the signal; re-establishment of homeostasis. The failure, therefore, to restore the redox steady state constitutes a condition of altered homeostasis and is seen as decreased health condition; it paves the way for the stimulation of another nuclear activator (NfKb) which exerts its proinflammatory activity on the nucleus by stimulating numerous genes to produce proinflammatory cytokines and interleukins (9). There is also genetic regulation of inflammation through receptors and mediators including toll-like receptor 4, TNF-alpha and -beta.

EFFECTS ON THE CHILD

The child is more susceptible to air pollution than the adult because, although the diameter of the pediatric airways is smaller and the tidal volume is less than that of the adult, the respiratory rate is much higher (27 ± 4 breaths per minute in the first 3 years of life, compared with 15 breaths per minute at 18 year of age) and therefore the amount of air ventilated in one minute when related to body weight is much greater than that of adults. For these reasons, pre-school and school-age children inhale more pollutants per kilogram of body weight than adults (10). Furthermore, the respiratory system contains only 20% of the alveoli at birth which increase in number through linear growth.

Finally, the child's immunological system is relatively immature with greater susceptibility to respiratory infections, which worsen the effects of atmospheric pollution and vice versa.

Effects of atmospheric pollutant exposure in pregnancy on the offspring

The studies carried out on pregnant women exposed to environmental pollution, measured through surveys of motoring stations distributed throughout relevant country, have given worrying results about the effects on the fetus and newborn baby.

A review of 13,775 pregnancies in Scotland, using scans performed in the 1st, 2nd, 3rd trimester of pregnancy found that exposure to higher levels of PM-2.5, PM-10, and NO2 were associated with lower infant head size during pregnancy and at birth (11).

A multicenter study in Canada, utilizing scans across all trimesters of pregnancy, reported that the risk of intrauterine fetal growth retardation was increased among women exposed to relatively low levels of am-

Table 2. *Main effects of air pollutant on human health.*

Immunological: inhibition of interferon-gamma synthesis, stimulation of Th2 and Th17 immunity.
Upper airways: < mucociliary clearance, < antioxidant
Cardiovascular: dysregulation of automatic system.
Pulmonary: production of ROS.
Epigenetics: DNA methylation, hystone acetylation,micro-RNA.

bient air pollutants (CO, NO2, and PM-2.5) in urban areas during pregnancy (12).

A meta-analysis that including nearly 3 million births across 14 centers from nine developed countries found that air pollution was associated with a higher risk of low-birth-weight infants. (13).

In a multicenter study performed in Spain on 1295 pregnant women, a correlation was demonstrated between levels of environmental exposure to benzene and NO2 in pregnancy and the airflow obstruction in the offspring in the preschool age (14).

Traffic pollution and child health

Ultrafine particles generated by traffic emissions have been suggested to have particularly bad effects in the airways due to a high level of pulmonary deposition and their ability to induce inflammation and oxidative stress (15).

A questionnaire study involving the parents was carried out on 2490 children aged 3 to 6 in the kindergartens of Changsha, capital of the province of Hunan in central-southern China, with a population of 7.22 million inhabitants, to investigate doctor-diagnosed asthma in preschool children and its relationship with exposure to ambient air pollution in pregnancy and during the first year of life. The result of this study was that the exposure to SO2 (as proxy of industrial air pollution), NO2 (as proxy of traffic pollution) and PM10 in utero and during the first year of life was associated with a higher risk of asthma attacks at 3-6 years of age compared with subjects living in low-exposure areas (16).

A Danish study examined the effect of exposure to air pollution on wheezing symptoms in children under the age of 3 years with genetic susceptibility to asthma. Significant positive associations were found between concentrations of PM-10, NO2, NO(x), CO and wheezing symptoms in infants (aged 0-1 year). Only the traffic-related gases [NO2, NO(x)] showed significant effects throughout the 3 years of life, albeit reducing after the age of 1 year (17).

Between 1999 and 2016 on the metropolitan region Utah's Wasatch Front 146,397 subjects with acute lower respiratory tract infections (ALRI) were studied. In the same period PM-2.5 air pollution concentrations were measured using community-based air quality monitors. The authors found that approximately 77% (n = 112,467) of subjects were 0-2 years of age. The odds of a health care encounter for ALRI for these young children increased within 1 week of elevated PM-2.5 and peaked after 3 weeks. This study demonstrated in a large sample of patients that short-term exposure to elevated PM-2.5 air pollution was associated with greater healthcare utilization for ALRI in young children, older children, and adults (18).

The distance of children's homes from traffic-intensive roads and the risk of wheezing in children has also been investigated.

In one paper it was found that the risk of wheezing episodes is greatest in children who live within 50 meters of a main road in the city (19). In another study, the risk was reportedly higher in children who live within 200 meters of a very busy road (*e.g.*, large ring roads) especially in children who had lived there for more than 2 years (20). Of course, these studies may be confounded by socio-economics status, the wealthy rarely live near major roads!

A multicenter study performed in Atlanta, Georgia, between 1993-2010 had demonstrated a close correlation between concentrations of air pollutants caused by traffic, ozone and PM-2.5 and visits to the Emergency Department for upper respiratory tract infections and pneumonia in children between 0-4 years of age (21).

In a prospective study, 1759 children (average age, 10 years) from schools in 12 southern California communities were recruited and their lung function measured annually for eight years. Over this period, deficits in the rate of increase of FEV1 were associated with exposure to NO2, acid vapor, PM-2.5, and elemental carbon (22).

The same authors subsequently studied three cohorts of children in 3 separate 4-year periods and found an increase in the rate of growth of spirometry in successive 4-year periods which correlated with the reduction of NO2 and of PM-2.5 and less than PM-10, associated with the implementation of air quality-control policies. Significant improvements in lung-function development were observed in both boys and girls and in children with and without an asthma diagnosis (23).

In a meta-analysis of 87 studies, other authors found that exposure, even for a short time, to atmospheric pollutants (O3, CO, NO2, SO2, PM-10 and PM-2.5)

resulted in an increased risk of emergency room visits and hospitalizations in asthmatic subjects. The risk was the same in children and older adults (24).

In a recent official ATS workshop on "Outdoor Air Pollution and New-Onset Airway Disease", the Epidemiology Group found that long-term exposure to air pollution, especially components of traffic-related air pollution such as nitrogen dioxide and black carbon, is associated with onset of childhood asthma. (25)

PROACTIVE INITIATIVES TO REDUCE THE RISKS FROM AIR POLLUTION

To improve air quality and reduce air pollution, which cannot be considered just a regional problem, but a global issue, the WHO issued guidelines in 2005 to reduce atmospheric pollutants and establish risk thresholds for the health of individuals.

In 2005 the Air Quality Guidelines (AQG) recommended not to exceed the concentration of PM-2.5 of 10 µg/m^3, and of NO2 of 40 µg/m^3, in built-up areas, giving no indication for ozone (O3).

After the lockdown of the COVID-19 pandemic period with the resumption of full-time industrial activities, road, air and sea traffic and the war that broke out on February 24TH, 2022 in Eastern Europe, which also caused, among other things, a huge dispersion of methane gas in the Baltic Sea (rupture of the Nord-Stream gas pipelines), the air pollution problem has returned beyond pre-lockdown levels.

Anyway in 2021, the WHO updated the previous guidelines recommending a further reduction of the previously recommended thresholds, indicating as an objective the average annual concentration of PM-2.5 not exceeding 5 µg/m^3, NO2 not exceeding 10 µg/m^3, and the peak seasonal average for 8 h of ozone not exceeding 60 µg/m^3 (**Table 3**) (26).

The reason for this drastic reduction of the thresholds for NO2, O3 and PM-2.5 is consequent on recent studies showing that the adverse effects of air pollution are not only limited to high exposures; harmful health effects can be observed at very low concentration levels, with no observable thresholds below which exposure can be considered safe (27).

These new guidelines have been signed by the Presidents of 109 Scientific Societies, Scientific Associations and Patients' Associations from all over the world.

While the guidelines are not legally binding, we hope that they will influence air quality policy across the globe for many years to come.

It is important that all pediatricians continue to advocate for measures to protect the fetus and child from atmospheric pollution, as well as treating the consequences.

Table 3. *2021 WHO Air Quality Guidelines Recommendations.*

Average annual concentration of PM-2.5 not exceeding 5 µg/m^3.
NO2 not exceeding 10 µg/m^3.
Seasonal average for 8 h of ozone (O3) not exceeding 60 µg/m^3.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interests

The Authors have declared no conflict of interests.

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Authorship

Professors Angelo Barbato, Andrew Bush.

Author contributions

ABa and ABu check the international medical databases (PUBMED, EMBASE, COCHRANE), wrote the paper and made the tables.

Ethical approval

Human studies and subjects

N/A.

Animal studies

N/A.

Data sharing and data accessibility

The data underlying this article are available in the article.

Publication ethics

Plagiarism

All original studies are cited as appropriate.

Data falsification and fabrication

All the data correspond to the real.

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