Air pollution: A threat to the health of our children

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Abstract
Background/methods: Current air pollution levels pose a threat to the health of children starting from conception. The scientific evidence is presented for mortality, morbidity, and sub-clinical effects. The first section deals with exposure data, the following sections with the evidence of health effects from epidemiology and toxicology leading to recommendations.

Results: Improved air quality reduces the number of infants’ deaths as well as disease and pain.

Conclusions: Medical doctors have a responsibility to know the facts and to advise their patients. Doctors when visiting their patients’ homes should be aware of the possibly grave impact of the indoor environment for the respiratory health of their patients. They should recognize and advise the parents on problems associated with environmental tobacco smoke, poor ventilation, mould growth, and maintenance of heating installations. With regard to outdoor air pollution, doctors could serve as role models and also advise their patients and parents on environmentally friendly behaviour. Such behaviour not only calls for personal commitment but also for the right infrastructure to be provided (e.g. public transport, district heating). Doctors should be proactive in the community and in their country as advocates for a healthier environment for our children.

Key Words: Children, environment, air pollution, health effects, exposure

Introduction

Outdoor air pollution is one of the most important environmental factors of childhood mortality and morbidity. This review will mainly focus on the primary ambient pollution mixture and also consider some aspects of the indoor environment where appropriate. However, the air is not only important as a direct exposure pathway. Especially persistent pollutants are often primarily emitted into the air but then contaminate the soil, water, and the food chain. While the main direct exposure route is via ingestion, the atmospheric transport of these substances should not be neglected. All these interesting aspects cannot be covered in this review because the direct effects of air pollution on children’s health are already noteworthy enough.

Not only do numerous studies show that poor air quality is detrimental to childhood health, but also some studies prove the positive effects of improved air quality. In the seminal study of the Utah Valley in 1987, when a steel mill was closed and air quality improved, significantly Pope [1,2] found a reduction of childhood hospital admissions to nearly one-third compared with the previous and the following year. The improved air quality in East Germany after reunification led to a tremendous reduction in non-allergic respiratory symptoms [3] and improved lung function [4] in schoolchildren. The same was also seen in an Austrian study in the industrial town of Linz [5] and in Switzerland [6].

Avol et al. [7] studied more than 100 children who had moved from one community to another between
the age of 10 and 15 years. Children who had moved to areas of lower particulate matter concentration (PM10) showed increased growth in lung function compared to those who moved to communities with higher PM10.

During the Olympic Games in 1996, the city of Atlanta was closed for individual motor traffic and consecutively air pollution and especially ozone levels dropped significantly. In parallel, the frequency of asthma admissions was reduced by approximately 40%, while admissions due to acute non-respiratory events did not change substantially [8].

Taken together, these are relatively few studies evaluating the effects of reduced air pollution on children’s health. Nevertheless, they show that reduced exposure to air pollutants can lead to a decrease in hospital admissions for respiratory complaints, a lower prevalence of bronchitis and respiratory infections, and improvements in impaired lung function growth rates. The results provide some direct evidence that reducing exposures to air pollution will improve children’s health.

**Exposure**

**What are the pollutants?**

Air pollution consists of a mixture of many compounds, generated by different sources. Its composition varies between different locations and also displays temporal variations within the same geographical area. Since it is impossible to monitor each component of this mixture, ‘indicators’ are used to assess air pollution exposure and health effects; the concentration of these indicators is used to represent the ambient pollution mixture as an exposure surrogate [9].

There are different distinct groups of indicator pollutants: the first consists of particulate pollution (e.g. black carbon, PM10, total suspended particles, TSP), nitrogen oxides (NOX), and carbon monoxide (CO). These compounds are closely correlated with each other (both temporally and spatially) and serve as indicators for primary pollutants from (fossil) fuel burning. Particles are also generated as secondary pollutants from semi-volatile compounds or through chemical reactions of gaseous pollutants in the atmosphere. NO2 mostly forms in the atmosphere under the impact of O2 from NO and thus reaches highest concentrations at some distance from main point sources. CO oxidizes to CO2. Thus, all these indicators differ in their spatial and temporal variability. They are not equally good indicators for each study setting; the choice depends on the health outcomes to be studied, the spatial distribution of the study population, and the chosen averaging time for the pollutants’ concentration.

Another important group of pollutants with its indicator ozone (O3) is derived from some of the above mentioned primary pollutants through chemical processes. These involve the action of sunlight (solar UV radiation) on nitrogen dioxide and hydrocarbons.

These two pollution mixtures are most relevant for the ambient air quality. However, sometimes other exposure scenarios are relevant. For example, some industrial point sources emit quite specific toxic compounds. Also agricultural activities and waste disposal facilities can cause typical pollution profiles that differ from the usual mixtures. A very special setting is the indoor environment. Indoors, some reactive chemicals such as ozone will usually not reach the high outdoor concentrations, but most outdoor pollutants will penetrate indoors and reach rather similar concentrations. Depending on various indoor sources (building materials, behaviour of the occupants such as smoking, etc.) and the ventilation rate, several pollutants are substantially more concentrated indoors than outdoors.

**How is the exposure situation in Europe?**

This question will be exemplified for the two important pollution indicators NOX and PM10.

**Nitrogen oxides (NOX)**

Nitrogen oxides are a side product of the oxidation processes. During combustion of all fuel types by elevated temperatures, oxidation of air nitrogen takes place. Another source of nitrogen oxides is direct combustion of nitrogen-containing fuels (biomass, coal, etc.).

There are two important nitrogen oxides occurring in the air. Nitrogen monoxide is the direct combustion product. In the atmosphere it reacts with oxygen to form nitrogen dioxide (NO2). This is one of the major components of air pollution in densely populated areas, mostly stemming from the combustion of fossil fuels in stationary sources (power generation, heating facilities) and motor vehicles.

According to the WHO [10], natural background annual mean concentrations are in the range 0.4–9.4 µg/m³. Outdoor urban levels have an annual mean range of 20–90 µg/m³ and hourly maxima in the range 75–1015 µg/m³. Urban outdoor levels vary according to the time of day, the season of the year and meteorological factors. Typical daily patterns show a low background level and one or two high level peaks that correspond to rush-hour traffic emissions of nitrogen oxides.

Usually indoor levels are rather similar to outdoor levels. However, with indoor sources such as unvented gas stoves or kerosene heaters the average
concentration over a period of several days may exceed 200 \( \mu g/m^3 \) (0.1 ppm). Maximum brief (min to 1 h) concentrations in kitchens are in the range 230–2055 \( \mu g/m^3 \) (0.12–1.09 ppm) during cooking with a gas stove. According to EEA [11], there is no clear trend over the last 10 years in the countries of the European Union, while until 1995 a downward trend was observed. Hotspots of European air pollution are shown in Figure 1.

**Particulate matter (PM)**

Particulate matter (PM) in ambient air is a complex mixture of multiple components ranging from a few nanometres in size to tens of micrometres. PM develops dynamically as a reactive system in time and space, depending both on sources and weather conditions. Primary particles originate from a multitude of natural and anthropogenic sources. Secondary particles derive from both the gaseous phase and from interactions with primary particles in a complex manner. Many toxic substances are found among the components present in ambient PM.

While the chemical composition influences the toxicology of a particle, its size (aerodynamic diameter) is the most important factor for the internal (inhalative) exposure.

Particles smaller than 10 \( \mu m \) (PM10) are able to reach the respiratory tract below the larynx. The coarse fraction (particles larger than 2.5 \( \mu m \)) mostly stems from the earth’s crust. The proportion of coarse particles in PM10 varies between locations.

Particles smaller than 2.5 \( \mu m \) (PM2.5) can penetrate into the gas-exchange region of the lung. Many of these particles develop through aggregation of ultrafine particles. In urban or industrialized areas they comprise 60–70% of the PM10 fraction and consist to a high degree of elemental carbon (soot) derived from stationary or mobile combustion sources.

Particles smaller than 100 nm (ultrafine fraction) are formed primarily through chemical or combustion processes, but some also as secondary particles from gaseous precursors in the atmosphere. In the urban environment ultrafine particles from vehicle emissions are reactive and tend to accumulate to form larger particles. Therefore their spatial variation is

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**Figure 1.** The image shows the European mean tropospheric nitrogen dioxide (NO2) vertical column density (VCD) between January 2003 and June 2004, as measured by the SCIAMACHY instrument on ESA’s Envisat. The scale is \( 10^{15} \) molecules/cm\(^2\). The image produced by S. Beirle, U. Platt and T. Wagner of the University of Heidelberg’s Institute for Environmental Physics. Credits: University of Heidelberg.
high and not well represented by routine monitoring networks. PM10 is regulated and routinely controlled in the European Union with limit values of 50 μg/m³ for the daily mean and 40 μg/m³ as annual average. At most of the monitoring stations the limit value for the annual average is met. However, in many urban areas and also in alpine basins and valleys the 50 μg/m³ limit is exceeded on many days per year. Routine monitoring with comparable techniques has to date only been performed for five years. Therefore it is not possible to report European-wide temporal trends. In some urban settings a decrease in the number and mass of coarse particles was observed, while the number of nanoparticles has increased at some locations [12]. In general, data on ultrafine particles are still limited [13]. It is accepted that particle pollution is inadequately regulated and controlled by PM10; the EU is introducing controls on PM2.5 but needs also to move on separate controls of ultrafine particle pollution. Additionally there are minor pollutants such as heavy metals, persistent chlororganic pollutants (POPs), and polycyclic aromatic hydrocarbons (PAHs) which are suspected of harming health but studies are still limited. Controls are being introduced on mercury and a limited list of POPs. PAHs are thought to be carried into the lung stuck to ultrafine particles, making it difficult to separate the contributions of each [14].

**Epidemiology**

**Impacts on pregnancy**

There is now substantial evidence concerning adverse effects of air pollution on different pregnancy outcomes. The evidence is suggestive of causality for the association of birth weight with air pollution, although further studies are needed. For preterm births and intrauterine growth retardation (IUGR), the current evidence is consistent with a causal relationship. Molecular epidemiological studies suggest possible biological mechanisms for the effect on birth weight, premature birth and intrauterine growth retardation, and support the view that the relationship between pollution and these pregnancy outcomes is genuine [14]. For birth defects, the evidence to date is insufficient to draw firm conclusions. Nevertheless, some findings indicate an effect [15].

Glinianaia et al. [16] reviewed the evidence on particulate air pollution and foetal health. They evaluated 12 studies from all over the world, including several studies from the Czech Republic. They restricted their objective to reductions in foetal growth, preterm birth, and stillbirth. There are only few studies that address these issues. Because the risk estimates are small, this number is not sufficient to draw conclusions concerning the precise amount of the added risk or the most vulnerable time window during pregnancy. In summary they call for more studies, which should also apply biomarkers such as PAH DNA-adducts.

Recent results [17–19] suggest that the first month is the most sensitive period for the effect of air pollutants but further studies should clarify this issue. The risk of IUGR is increased if monthly concentrations of PM10 exceed 40 μg/m³. Studies [18,20] imply a critical role of PAHs. It is possible that carcinogenic PAHs are responsible for the biological activity of complex mixtures adsorbed to respirable air particles that can result in IUGR. With the increase in traffic, the significance of PAHs in Europe is growing but their monitoring remains limited.

On the whole, these outcomes resemble those of pregnant women exposed to environmental tobacco smoke (ETS). This is a very specific indoor air pollutant mixture with some similarities to urban outdoor air pollution. A clear dose-dependent response is evident for tobacco smoke ranging from heavy (active) smoking of pregnant women to light smoking and only passive exposure. This adds confidence to the causality of the association between ETS exposure of pregnant woman and reduced foetal growth, preterm birth, and stillbirth (see review on ETS in this supplement). Considering the parallels between urban air pollution and ETS (fine particles with many toxic compounds from incineration sources), also the small effects of urban air pollution during pregnancy are probably causal.

Even small reductions in birth weight have a long-lasting impact later in life leading, e.g. to higher rates of coronary heart disease, hypertension, obesity, diabetes, and renal diseases [21–24], but also impacting mental development [25,26]. It is difficult to quantify effects on early pregnancy which might be the most susceptible period, because especially early pregnancy losses often go unnoticed. Air pollution exposure of pregnant woman not only impacts the pregnancy outcomes, but also the health of the child after birth which will be discussed in the next section.

**Health effects after birth**

**Infant mortality**

Increased child mortality was recorded during the great London smog of 1952, roughly a doubling for newborns under four weeks and infants under one year [27], but this was omitted from the official British report. Today, the large numbers of studies (e.g. [28], [29]) allows Bates [27] to conclude that air pollution does, in fact, kill and cripple children. The low child mortality in many parts of the world makes it difficult to reach statistically meaningful numbers and this has
been used till recent years to discount the evidence. The limited data suggest that a 10 µg/m³ increase in PM10 or NO₂ leads to some percentage increase in daily mortality where sudden infant death syndrome (SIDS) and death due to respiratory diseases are most affected; very young children, preterm and low birth-weight babies are most susceptible. In terms of exposure to specific pollutants, evidence is strongest for the relationships between particulate matter and infant deaths.

The World Health Organization [30] estimates that preventable outdoor air pollution (defined as annual mean levels of respirable particle concentration – PM10 – above 20 µg/m³) each year causes the death of approximately 5000 children aged zero to four years due to respiratory diseases in the whole WHO European Region (which includes the countries of the former Soviet Union). Most of these deaths are calculated for the subregion B. This subregion is defined by the adult mortality rate (very low adult mortality in subregion A, low in subregion B, and high in subregion C) and consists mostly of south-east European countries and some countries from the southern parts of the former Soviet Union. These countries are troubled by high air pollution and still comparatively high childhood mortality rates so that even moderate percentage increases in mortality lead to a substantial number of additional cases.

Respiratory symptoms and reduced lung function

Effects have been studied both in healthy children and in children with asthma or other chronic respiratory diseases. An increase of 10 µg/m³ (daily average) in PM10 or in NO₂ leads to approximately a 10% increase in incidence of asthma attacks and in nocturnal cough in asthmatic children. Asthmatic children without proper medication usually experience stronger effects, while anti-inflammatory medication ameliorates the effects of air pollution [31]. Even if effects in asthmatic children were of the same magnitude (percentage increase in symptoms prevalence per unit increase in pollutants concentration) as in healthy children, the background frequency of symptoms in healthy children is considerably lower, rendering asthmatic children more vulnerable.

There are several studies on lung function decrement due to air pollution. They provide ample evidence that there are acute effects in time series studies [32,33] and chronic effects when comparing cohorts [34–41] or longer time intervals [4] of air pollution on lung function and lung growth. Some studies looked at asthmatic subjects in panel studies [42–45]. The findings are supported by other studies that found health effects in children living near busy roads, measuring exposure not by analysing a specific pollutant but either by measuring distance to road or number of cars [46–52].

Changes in lung function parameters per 10 µg/m³ of PM10 short-term variation (time series panel studies) are in the magnitude of 1%, while long-term exposures (in cohort studies) yield somewhat stronger effect estimates. While, on average, these changes are small (and would not be clinically relevant if encountered in an individual), this small change in the population mean is equivalent to a considerable increase in the number of individuals with a clinically relevant reduction in lung function.

Although not every study found significant effects of air pollution on the rate of symptoms and lung function, on the whole there is consistency between the studies from various parts of the world with different concentrations of pollutants and with different study designs [53–66]. Many studies found significant effects and dose-effect associations, lending strength to the assumption of epidemiological evidence of causality. Findings in children are generally in accordance with findings in adults and in experimental studies, although possibly indicating a somewhat higher susceptibility in children.

Evidence is sufficient to infer a causal relationship between exposure to ambient air pollutants and adverse effects on lung function development. Both reversible deficits of lung function and chronically reduced lung growth rates and lower lung function levels are associated with exposure to air pollution, with clearer relationships for particulates and traffic-related air pollution. Findings of various population-based studies are supported by animal exposure studies, indicating that intrauterine as well as postnatal exposures to pollutants can lead to impaired lung growth.

The available evidence is also sufficient to assume a causal relationship between exposure to air pollution and aggravation of asthma (mainly due to exposure to particulate matter and ozone) as well as a causal link between increased prevalence and incidence of cough and bronchitis due to particulate exposure. There is little evidence for a causal association between asthma prevalence/incidence and air pollution in general, although the evidence is suggestive of a causal association between the prevalence/incidence of asthma symptoms and living in close proximity to traffic.

Compared with many other pollutants, ozone, an irritant gas, is widely investigated both through epidemiological and toxicological studies. In general, the mechanisms of action are clear. Reviews focus on the toxicological basis of the US National Ambient Air Quality Standard for ozone [67], on ‘ozone and the lung’ [68], on lung inflammation and mucosal barrier disruption [69], and on the effects of ozone in the context of the sensitivity of the postnatal lung to
environmental insults and oxidant stress [70]. Children and asthmatics show more ozone-related acute lung function decrements than other population subgroups [71]. Asthmatic children with a genetic deficiency of GSTM1 may be more susceptible to the effects of ozone on their small airways and they might benefit from antioxidant supplementation (vitamin C and E) [72].

Long-term effects of ozone on lung growth were found in the United States [73], while European investigators only found medium-term, but not long-term effects (the study period was 3.5 years) on the lung growth of schoolchildren [74]. This could be due to differences in the amount and specific composition of the oxidative pollutants’ mixture, but also to the longer duration of the American study.

Reduction of road traffic in Atlanta during the Olympic Games resulted in a decrease of ozone concentrations and significantly lower rates of childhood asthma events [8]. These data provide support for efforts of politicians to improve health by means of reductions in motor vehicle traffic. Public health benefits (in general) from a reduction of ozone concentrations have been assessed by Levy et al. [75].

To our knowledge, only one study on the impact of ultrafine particles on children has been published to date. Pekannen et al. [76] investigated the variations in PEF in Finnish asthmatic children. The association of nanoparticles was not stronger than with PM10 or Black Smoke. In healthy children the percentage of alveolar macrophages containing nanoparticles ranged from 1% to 16% per child [77]. The percentage of particle-containing alveolar macrophages did not change with age, but was higher in children living near a main road compared with those living on a quiet residential road.

Hospitalization for respiratory diseases and emergency visits

In time series studies a 10 μg/m³ increase of NO₂ or PM10 (daily mean) leads to a few percentage increase in daily hospital admissions of children due to respiratory diseases [78–82]. Cohort studies yield somewhat stronger effect estimates. Also, when considering cumulative exposure over several days in time series studies the effect estimates tend to be higher. Children seem to be more sensitive than adults and among children the younger ones (below two years of age) are most sensitive.

Allergies

Allergies are one of the real ‘new epidemics’. Globally, the ISAAC study [83,84] demonstrated a wide range in rates for symptoms of asthma, allergic rhinitis and eczema. For asthma symptoms (wheeze) in the previous 12 months in 13–14-year-old children, up to 15-fold differences were found between countries, ranging from approximately 2–3% in Albania, China, Greece, Indonesia, Romania and the Russian Federation, to approximately 30% in Australia, New Zealand, Ireland and the United Kingdom. The results of the questionnaire-based ISAAC study were supported by results from ISAAC phase II surveys, which included objective markers of atopy such as skin prick test reactivity, and measures known to be strongly associated with asthma, such as bronchial hyper-reactivity [85,86].

The change in prevalence of wheeze and asthma over time in Europe was addressed in a number of investigations using identical methodology, repeated after a period of time [87]. Most surveys found a significant increase in childhood asthma in ‘western affluent’ countries over the last few decades, with a trend ranging from only a slight increase up to a three-fold increase [88–92].

In addition to a strong genetic component, several factors were related to the prevalence of asthma and atopic diseases in many studies. These included infections early in life, microbial exposure, allergen exposure, family size, socioeconomic factors, and nutrition. Increased exposure to livestock was related to a decreased risk for atopic diseases [93,94]. Exposure to stables and farm milk starting very early in life appears to have a strong protective effect against the development of asthma, hay fever and atopic sensitization [95]. Certain components (lipopolysaccharides) of the cell wall of Gram-negative bacteria, which were found to be more prevalent in farming environments, were suggested to be involved in the modulation of the immune system, possibly protecting against the development of atopy [96].

However, also indoor and outdoor air pollution and environmental tobacco smoke seem to contribute to asthma and allergy. This is certainly true for the enhancement of symptoms in asthmatic subjects [97,98], but a growing body of evidence also indicates that chemical irritation leads to (sub-) cellular damage of the airways and especially in early life can contribute to the shift of the immune system to an atopic state. Thus pollutants can enhance allergic sensitization in those genetically at risk, lending plausibility to the role of potentially injurious effects of air pollutants in the causation of paediatric lung disease, including asthma. The possible mechanisms of these effects need further research.

Children with atopic dermatitis are more at risk for asthma if exposed to environmental tobacco smoke than children without dermatitis [99]. In the United States, 380 000 excess cases of childhood asthma and wheezing equalling 7.5% of all symptomatic children [100] have been attributed to maternal smoking. Most studies report adverse effects of
parental smoking on asthma in infancy and early childhood, while the effects of past and current exposure to environmental tobacco smoke on the incidence and persistence of wheeze and asthma in adolescence are less clear. This, however, may be partially explained by parents changing their smoking behaviour due to their children having asthma, reporting bias and other methodological limitations, and to the natural history of asthma overlapping the effects of passive smoking.

Evidence is conflicting on the association between exposure to environmental tobacco smoke and atopic sensitization in childhood. In two studies, increased allergic sensitization [101] and an enhanced prevalence of eosinophilia [102] were found in relation to parental smoking, while other investigators did not confirm these findings [103–105].

A cohort study reported an increased risk of developing asthma in children who played at least three sports outdoors in areas with high ozone levels compared with children playing no sports [73]. Krämer et al. [106] found that hay fever, symptoms of allergic rhinitis, wheezing, sensitization against pollen, house dust mites or cats, and milk or eggs were associated with outdoor NO2. The results indicate that traffic-related air pollution leads to increased prevalence of atopic sensitization, allergic symptoms, and diseases.

Typical indoor pollutants have been associated with increased prevalence of asthma and allergy including formaldehyde [107–110], cleaning products [111], solvents [112–114], and moulds [115–118].

Another interesting mechanism linking allergies to air pollution is the impact of air pollution on pollen that is subject to physicochemical alterations in polluted air. When pollen comes into contact with soot and other dust particles (especially in humid conditions such as in the respiratory tract) they tend to burst and allergens stick to the smaller particles’ surfaces. Pollen counts and pollen allergens measured in fine particles are correlated [119,120]. The chemical composition of air pollutants also stimulates the release of proinflammatory eicosanoid-like substances from pollen grains [121].

Growth rate, mental and physical development, and other health effects

Epidemiological data for these outcomes are limited. Reduced growth rate would be a chronic exposure’s effect calling for cohort studies comparing different regions. However, this design is prone to bias due to other regional differences (e.g. nutrition, socioeconomic status, genetic influences) that also impact the growth rate. With regard to the mental and physical development of children, also exposure to specific pollutants such as heavy metals, persistent organic pollutants (POPs), and polycyclic aromatic hydrocarbons (PAHs) and other events before birth must be considered. One paper [122] even reported that increased ozone exposure may be a contributory factor in the development of type 1 diabetes in children.

Summary

Relative risk estimates for the health outcomes reviewed are generally small. However, reductions in lung function seem to persist to adulthood and lifetime risks due to harm in childhood are largely unknown. Nevertheless, owing to the widespread nature of the exposure and the relatively high incidence of many of the relevant outcomes, the population attributable risks are noteworthy, i.e. the amount of ill-health attributable to air pollution among European children is high. While recognizing the need for further research, current knowledge on the health effects of air pollution is sufficient to strongly recommend that children’s current exposure to air pollutants be reduced, particularly in regard to traffic-related pollutants.

Children with underlying diseases such as asthma might be especially susceptible to air pollution in regard to inflammatory responses. On the other hand, a good therapeutic regime is able to counterbalance also the ill-effects of the pollution. Air pollution increases the risk of low birth weight. At the same time babies with low birth weight are at a higher risk from air pollution episodes. This includes several outcomes ranging from respiratory diseases to SIDS. It should be recognized that air pollution significantly affects children’s health from the time of conception.

Toxicology

Because of the multitude of compounds that interact in the atmosphere and in the human body, toxicology is less well adapted to guide risk assessments in the field of air pollution. Nevertheless, toxicological findings can add to the understanding of the mechanisms leading to the associations observed in epidemiological studies. Especially the effects of particulate pollution have been intensively studied recently and are discussed in this section.

Inhalation of PM exacerbates the symptoms of pre-existing lung disease such as asthma, as well as heart and blood vessel diseases. Toxicological studies show that these effects are mediated by mechanisms such as lung inflammation, heart rate variability, changes in blood viscosity and oxygen deprivation.

Cellular models provide important mechanistic information about how various particles and components relevant to air pollution interact with cells and cellular systems. The studies describe inflammatory
responses that may be important in the adverse effects seen following increases in exposure to particulate matter. The studies provide support for the theory that very small particles (nanoparticles) are an especially harmful component, but also suggest that the more coarse and intermediate-size PM is important, too. There are questions about the common use of PM mass as a description of the severity of pollution, since PM number, size and chemical composition of the PM mix are clearly important in driving biological endpoints in addition simply to PM mass [123].

The use of in vitro (cellular and other non-animal) systems is a valuable addition to the repertoire of toxicological models. In vitro research is primarily directed towards studying early events and dissecting cellular and molecular pathways. Among the cells that respond to particles are those that form the primary line of defence in our respiratory system, the macrophages. The epithelial barrier cells that line the air spaces of the lung also encounter particles and are important in inflammation and defence [124].

The inflammatory response plays a central role in the adverse effects of PM and in pre-existing airways disease such as asthma and chronic obstructive lung disease, as well as in subjects with heart and circulatory diseases. Therefore, toxicologists interested in this aspect study the inflammatory effects of PM. In contrast, toxicologists interested in elaborating the role of PM in cancer, study DNA effects such as mutations, DNA breakage and adduct formation (irreversibly bound material). For both inflammatory and mutagenic effects, highly reactive compounds such as polycyclic aromatic hydrocarbons (PAHs) or transition metals on the surface of ultrafine particles play an important role.

The molecular epidemiological studies suggest biological mechanisms for the effect of air pollution on birth outcomes. It has been shown that the levels of DNA adducts are positively related to risk of IUGR [18,125], birth weight, birth length and head circumference [126,127], and hypoxanthine-guanine phosphoribosyl-transferase locus (HPRT) mutation frequency in infants [128]. The increase in the levels of DNA adducts related to pollution is similar to, but smaller in magnitude than the differences between smoking and non-smoking mothers. All this indicates that ambient air pollution levels do translate to higher individual exposures, even for unborn babies. The molecular epidemiology studies, and the similarity of effects of air pollution to those of smoking, support the biological plausibility of the effects.

Studies on rodents demonstrate that ultrafine particles administered to the lung cause a greater inflammatory response than larger particles, compared on a mass basis [129]. Surface properties/surface chemistry seem to play an important role in ultrafine particle toxicity. It has to be borne in mind that the large surface area of ultrafine particles provides an interface for catalytic reactions of surface-located agents with targets such as proteins, cells, etc. [130]. In addition, ultrafine particles show a high deposition in the lung [129]. They can induce oxidative stress, influence cell signalling and can lead to the release of mediators initiating inflammatory processes not only in the respiratory tract but also in the cardiovascular system [130]. However, these toxicological studies do not really simulate the long-term exposure of (susceptible) humans in urban environments.

Ultrafine particles can escape alveolar macrophage surveillance and gain access to the pulmonary interstitium [129]. They can translocate to other organs, even the brain [131]. In rats, pulmonary inflammation and oxidative stress was modified by age, copollutants, and a compromised respiratory tract. Carbon and ozone interacted such that reactive oxygen species (ROS) activity was depressed in young rats, whereas it was enhanced in old rats [132].

Exposure of 10-day-old rat pups to soot and iron particles in the size range of 10 to 50 nm had no effect on the rate of cell proliferation within terminal bronchioles or the general lung parenchyma. However, when looking at the reported effects of diesel exhaust such as increased risk of allergy, it has to be considered that diesel exhaust is a mixture of many pollutants [135]. A recent review on the effects of traffic-related pollutants, especially of diesel exhaust particles, on allergic disease has been published by Heinrich and Wichmann [136].

It should be noted that diesel engines emit large numbers of ultrafine particles. The reduction of these emissions is of high priority. However, when looking at the reported effects of diesel exhaust such as increased risk of allergy, it has to be considered that diesel exhaust is a mixture of many pollutants [135].

Interestingly, the impact of ultrafine particles from nanotechnology (termed nanoparticles) has been underestimated for a long time. Reviews on health and environmental impacts of nanotechnology have been published recently [137–140]. Nanoparticles are designed for their specific properties and often exhibit a profound biological activity. Nanoparticles penetrate between cells to enter the blood stream and organs; they pass through the openings in the natural membranes which separate body compartments and they appear to cross the placenta and so pose a particular risk to the foetus.
Recommendaons

Air pollution is a threat to the health of our children and the very young, and those with underlying diseases such as asthma are at increased risk to suffer from its impact. However, doctors can help. A good anti-inflammatory therapeutic regime in asthmatic patients helps to ameliorate the acute effects of pollution episodes and most probably also is a safeguard against chronic effects.

Doctors when visiting their patients’ homes should be aware of the possibly grave impact of the indoor environment for the respiratory health of their patients. They should recognize and advise the parents on problems associated with environmental tobacco smoke, poor ventilation, mould growth, and maintenance of heating installations.

With regard to outdoor air pollution, doctors could serve as role models and also advise their patients and their parents about environmentally friendly behaviour. As an example, walking and cycling, not only in respect to urban air quality, is better than travelling by car. As a routine part of daily physical activity it could also directly improve the health and well-being of every person.

Environmentally friendly behaviour not only calls for personal commitment but also for the right infrastructure to be provided (e.g. public transport, district heating). Doctors should be proactive in the community and in their country as advocates for a healthier environment for our children.

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