Epidemiology of Fine Particulate Air Pollution and Human Health: Biologic Mechanisms and Who's at Risk?

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This article briefly summarizes the epidemiology of the health effects of fine particulate air pollution, provides an early, somewhat speculative, discussion of the contribution of epidemiology to evaluating biologic mechanisms, and evaluates who's at risk or is susceptible to adverse health effects. Based on preliminary epidemiologic evidence, it is speculated that a systemic response to fine particle-induced pulmonary inflammation, including cytokine release and altered cardiac autonomic function, may be part of the pathophysiologic mechanisms or pathways linking particulate pollution with cardiopulmonary disease. The elderly, infants, and persons with chronic cardiopulmonary disease, influenza, or asthma are most susceptible to mortality and serious morbidity effects from short-term acutely elevated exposures. Others are susceptible to less serious health effects such as transient increases in respiratory symptoms, decreased lung function, or other physiologic changes. Chronic exposure studies suggest relatively broad susceptibility to cumulative effects of long-term repeated exposure to fine particulate pollution, resulting in substantive estimates of population average loss of life expectancy in highly polluted environments. Additional knowledge is needed about the specific pollutants or mix of pollutants responsible for the adverse health effects and the biologic mechanisms involved. *Key words*: air pollution, cardiopulmonary disease, health effects, life expectancy, particulate pollution, review. — *Environ Health Perspect* 108(suppl 4):713–723 (2000). *http://ehpnet1.niehs.nih.gov/docs/2000/suppl-4/713-723pope/abstract.html*

It has long been known, or at least suspected, that there are adverse health effects associated with ambient air pollution (*1*). Extreme air pollution episodes in the 1930s–1950s were associated with dramatically elevated cardiopulmonary morbidity and mortality. Evidence of serious health effects provided by these episodes spurred a growing concern about air pollution and in the United States during the 1950s through early 1970s, there was a series of legislative efforts related to trying to control air pollution. Current air pollution legislation is based largely on the 1970 Clean Air Act and 1990 Amendments to this act (*2*). The amended Clean Air Act mandated national ambient air quality standards for pollutants that are relatively common and widespread but may reasonably be anticipated to endanger public health. Six pollutants that met these basic criteria (criteria pollutants) were eventually selected, including particulate matter (PM), sulfur dioxide, nitrogen dioxide, carbon monoxide, ozone, and lead.

Since 1970 there have been hundreds of published studies that have evaluated the health effects of these air pollutants. A 1996 review of the health effects of these criteria pollutants (along with two other common pollutants) was prepared by the Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society (ATS) (*2*). There have also been numerous recent reviews that have focused on health effects of particulate air pollution (*3–14*). This article does not attempt to replicate the excellent ATS review of all the criteria pollutants or previous general reviews of particulate air pollution. The overall plan of this article is to focus on three basic topics. First, the epidemiology of the health effects of fine particulate air pollution $PM_{2.5}$ (particles ≤ 2.5 µm) will be briefly summarized, although recent, more comprehensive reviews are available. This summary relies heavily on updates of several previous reviews by Dockery and Pope (*6,8–11*). Second, a somewhat speculative discussion of the early but clearly incomplete contribution of epidemiology to evaluating the biologic mechanisms is provided. This discussion of biologic mechanisms is updated from papers originally prepared for presentation at international symposia (*10,11*). Finally, an original discussion of who risks adverse health effects due to exposure to fine particulate air pollution is presented.

Characteristics of Fine Particles

Particulate air pollution refers to an air-suspended mixture of solid and liquid particles that vary in size, composition, and origin. The size distribution of total suspended particles (TSPs) in the atmosphere is trimodal and includes coarse particles, fine particles, and ultrafine particles. Coarse particles (often defined as those with an aerodynamic diameter > 2.5 µm) are often naturally occurring and derived primarily from soil and other crustal materials. Fine particles ($PM_{2.5}$) are derived chiefly from combustion processes in transportation, manufacturing, power generation,

etc. Sulfate and nitrate particles are commonly generated by conversion from primary sulfur and nitrogen oxide emissions, and a varying portion of sulfate and nitrate particles may be acidic. Therefore, in most urban areas, $PM_{2.5}$ mostly comprises primary combustion-source particles as well as secondary combustion particles including sulfates and nitrates. Ultrafine particles are often defined as particles < 0.1 µm. These particles have relatively short residence times in the atmosphere because they accumulate or coagulate to form larger fine particles.

Various physiologic and toxicologic considerations suggest that exposure to fine particles may be a health concern. Their size is such that they can be breathed most deeply in the lungs. They include sulfates, nitrates, acids, metals, and carbon particles with various chemicals adsorbed onto their surfaces. Relative to coarse particles, they more readily penetrate indoors, are transported over longer distances, and are somewhat uniform within communities, resulting in highly ubiquitous exposure.

The initial reference method for measuring particle concentrations and establishing health standards in the United States was TSPs. In 1987 the U.S. Environmental Protection Agency (U.S. EPA) changed the reference method to include only inhalable particles. Inhalable particles refers to those particles that can penetrate the thoracic airways; for purposes of standard setting, inhalable particles were specifically defined as particles ≤ 10 µm in aerodynamic diameter (PM_{10}). In 1997 the U.S. EPA promulgated new standards (*15*) for an even finer cut of particulate air pollution—particles ≤ 2.5 µm in aerodynamic diameter ($PM_{2.5}$); however, in May 1999, a U.S. Court of Appeals blocked the implementation of these standards.

Health Effects of Acute Exposure

The large majority of epidemiologic studies of particulate air pollution have been acute exposure studies that evaluated short-term

(usually daily) variations in health end points such as mortality counts, hospitalizations, symptoms, and lung function associated with short-term variations in levels of pollution. A brief summary of the results of these acute exposure studies is presented in Table 1. Unfortunately, until recently (following the promulgation of the new $PM_{2.5}$ standards), there has been very little daily monitoring of fine particles, and most of the studies summarized in Table 1 used alternative measures of particulate concentrations.

Episode Studies

The earliest and most methodologically simple epidemiologic studies are those that evaluate air pollution episodes. These studies compare mortality (and morbidity) before, during, and after pollution episodes. In December of 1930 in the Meuse Valley, Belgium, in October of 1948 in Donora, Pennsylvania, and in December of 1952 in London, England, stagnant air masses resulted in marked increases in the concentrations of air pollutants. Although the biologic mechanisms were not well understood, the large excess mortality and morbidity associated with the extreme episodes clearly

demonstrated a link between mortality and morbidity and air pollution. During these episodes of highly stagnant air conditions, the PM pollution would have been primarily from combustion sources, and therefore PM mass would have been mostly fine particles. Two recent studies of less severe air pollution episodes (16,21) suggested smaller mortality and morbidity effects associated with less extreme pollution.

Mortality Counts

Many recent daily time-series mortality studies have also observed changes in daily death counts associated with short-term changes in particulate air pollution, even at relatively low or moderate concentrations (Table 1). There have been more than 60 such studies conducted in at least 35 cities. The relative risk of mortality increased monotonically with particulate concentrations, usually in a linear or near-linear fashion. These studies did not observe a particulate pollution health effects threshold. In addition, these studies often observed a lead-lag relationship between air pollution and mortality. The results suggested that the increased mortality occurred concurrently or within 1–5 days following an

increase in air pollution. Because various measurements of particulate pollution were used in the different studies, and because various modeling strategies were used, precise comparisons of effect estimates across all the studies were difficult. However, changes in daily mortality associated with particulate air pollution were typically estimated at approximately 0.5–1.5%/10 $\mu g/m^3$ increase in PM_{10} concentrations, or per about 5 or 6 $\mu g/m^3$ increase in $PM_{2.5}$ concentrations.

Studies that provided a breakdown of mortality by broad cause-of-death categories observed that particulate air pollution generally had the largest effect on respiratory and cardiovascular disease mortality. Estimates of daily mortality effects of an increase in exposure to particulate air pollution by broad cause-of-death categories are summarized in Table 2. The estimated cause-specific increase in mortality risk is much larger for respiratory than for cardiovascular disease. However, the percent of excess deaths attributable to particulate exposure is mostly due to cardiovascular disease.

Hospitalizations

Daily counts of hospital admissions can be analyzed in a manner similar to the assessment of daily counts of mortality. More than 50 daily time-series studies have reported associations between particulate air pollution and hospitalization or related health care end points (Table 1). Most of these studies have evaluated associations between respiratory hospital admissions and air pollution. Several studies have also analyzed emergency department visits for asthma, chronic obstructive pulmonary disease, and other respiratory ailments, and observed associations with particulate air pollution. More recent studies have observed associations between particulate air pollution and hospitalizations for cardiovascular disease (73,74,87,98–100).

Symptoms/Lung Function

There are more than 40 published studies evaluating associations between daily respiratory symptoms and/or lung function and particulate air pollution (Table 1). Although many of these studies focused on asthmatics and exacerbation of asthma, others followed nonasthmatics and evaluated changes in acute respiratory health status more generally. Small, often statistically insignificant, associations between particulate pollution and upper respiratory symptoms were observed. Associations with lower respiratory symptoms and cough, however, were typically larger and usually statistically significant. Exacerbation of asthma, based on recorded asthma attacks or increased bronchodilator use, were also associated with particulate air pollution. Associations between more general measures

Table 1. Summary of epidemiologic evidence of health effects of acute exposure to particulate air pollution.

Health end points	Basic study design	Observed associations with PM	References
Episodes of death and hospitalizations	Evaluate changes in mortality and morbidity before, during, and after pollution episodes.	Elevated respiratory and cardiovascular mortality and hospitalizations.	(16–21)
Mortality	Population-based time-series studies that include statistical time-series modeling to evaluate potential associations with daily mortality counts.	Elevated daily respiratory and cardiovascular mortality counts. Effects persisted with various approaches to control for time trends, seasonality, and weather. Near-linear associations with little evidence of a threshold.	(22–66)
Hospitalization and other health-care visits	Population-based time-series studies that evaluate associations between pollution and daily changes in hospitalization and related health-care end points.	Elevated hospitalizations, emergency visits, and clinic/outpatient visits for respiratory and cardiovascular disease. Effects generally persisted with various approaches to control for time trends, seasonality, and weather.	(67–114)
Symptoms/ lung function	Panel-based time-series studies of symptom and/or lung function data repeatedly collected from individuals in well-defined panels or cohorts.	Increased occurrence of lower respiratory symptoms, cough, and exacerbation of asthma. Only relatively weak associations with upper respiratory symptoms. Small, statistically significant declines in $FEV_{0.75}$, FEV_1, or PEF, and increased occurrence of clinically significant declines in lung function.	(115–152)

Abbreviations: $FEV_{0.75}$, forced expiratory volume in 0.75 sec; FEV_1, forced expiratory volume in 1 sec; PEF, peak expiratory flow.

Table 2. Overall estimates of daily mortality effects of an increase in exposure to particulate air pollution by broad cause-of-death categories.

Cause of death	Percent of total deaths[a]	Cause-specific percent increase per 50 $\mu g/m^3$ increase in $PM_{2.5}$[a]	Percent of excess deaths due to PM exposure
All causes[b]	100	7.0	100
Respiratory	8	25.0	28
Cardiovascular	45	11.0	69
Other disease	47	0.4	3

[a]Based on updated summary estimates from previous reviews (6,8,10). [b]Excluding accidents, suicide, homicide, etc.

of acute disease have been studied, including evaluations of the timing of restricted activity days of U.S. adult workers due to illness (131,132) and school absences in grade school children (141).

Measures of lung function have also been used as an objective and potentially sensitive indicator of acute response to air pollution. Various studies have taken repeated measurements of the lung function of panels of children and/or adults. These studies have typically reported very small but often statistically significant decreases in lung function associated with elevated levels of particulate air pollution concentrations. Lagged effects of up to 7 days were observed.

Effects of Chronic Exposure

The previously discussed acute exposure studies indicate that short-term exposures to elevated particulate air pollution are associated with short-term changes in cardiopulmonary health. These acute exposure studies provide little information about how much life is shortened, how pollution affects longer-term mortality rates, or pollution's potential role in the process of inducing chronic disease that may or may not be life threatening. Chronic exposure studies evaluate health end points across communities or neighborhoods with different levels of average pollution over longer time periods (usually 1 year or more). Chronic exposure studies attempt to evaluate the effects of low or moderate exposure that persists for long periods as well as the cumulative effects of repeated exposure to substantially elevated levels of pollution. A brief summary of the results of the chronic exposure studies is provided in Table 3.

Mortality Rates

Several population-based, cross-sectional mortality studies have evaluated associations between annual mortality rates and particulate air pollution across U.S. metropolitan areas (Table 3). The basic conclusions from these population-based cross-sectional studies were that mortality rates were associated with air pollution, and they were most strongly associated with fine or sulfate PM. Such associations are illustrated in Figure 1. Age, sex, and race-adjusted population-based mortality rates for U.S. cities in 1980 are plotted over various indices of particulate air pollution [obtained from Lipfert et al. (158) and U.S. EPA (163)]. Although much apparently stochastic variability exists, adjusted mortality rates are positively correlated with fine (PM$_{2.5}$) and sulfate particles but not with TSPs. Multiple regression modeling techniques to evaluate cross-sectional differences in air pollution and mortality and to control for other ecologic variables have been used.

Whereas the population-based cross-sectional studies from the United States dealt with total mortality, a study from the Czech Republic focused on infant mortality (154).

Infant mortality, especially respiratory postneonatal infant mortality, was strongly associated with particulate air pollution. All of these population-based cross-sectional

Table 3. Summary of epidemiologic evidence of health effects of chronic exposure to particulate air pollution.

| Health end points	Basic study design	Observed associations with particulate pollution	References
Mortality rates	Population-based cross-sectional analysis of mortality rates across communities with different levels of pollution.	Higher mortality in areas with higher fine particulate and/or sulfate pollution levels. Pollution effect sensitive to model specification and choice of covariates included in the analysis.	(153–160)
Survival/life expectancy	Cohort-based cross-sectional studies that link community-based air pollution data with individual risk-factor and survival data.	Increased risk of respiratory and cardiovascular mortality in adults, and respiratory and sudden infant death syndrome mortality in infants, even after controlling for individual differences in cigarette smoking and various other risk factors.	(161–164)
Disease	Cross-sectional studies of community air pollution with individual symptom/disease data from surveys or collected cohorts.	Increased chronic cough, bronchitis, and chest illness (but not asthma).	(165–170)
Lung function	Cross-sectional studies of community ambient air pollution data with individual lung function data from national surveys or collected cohorts.	Particulate air pollution associated with small but often statistically significant declines in various measures of lung function in both children and adults.	(171–176)
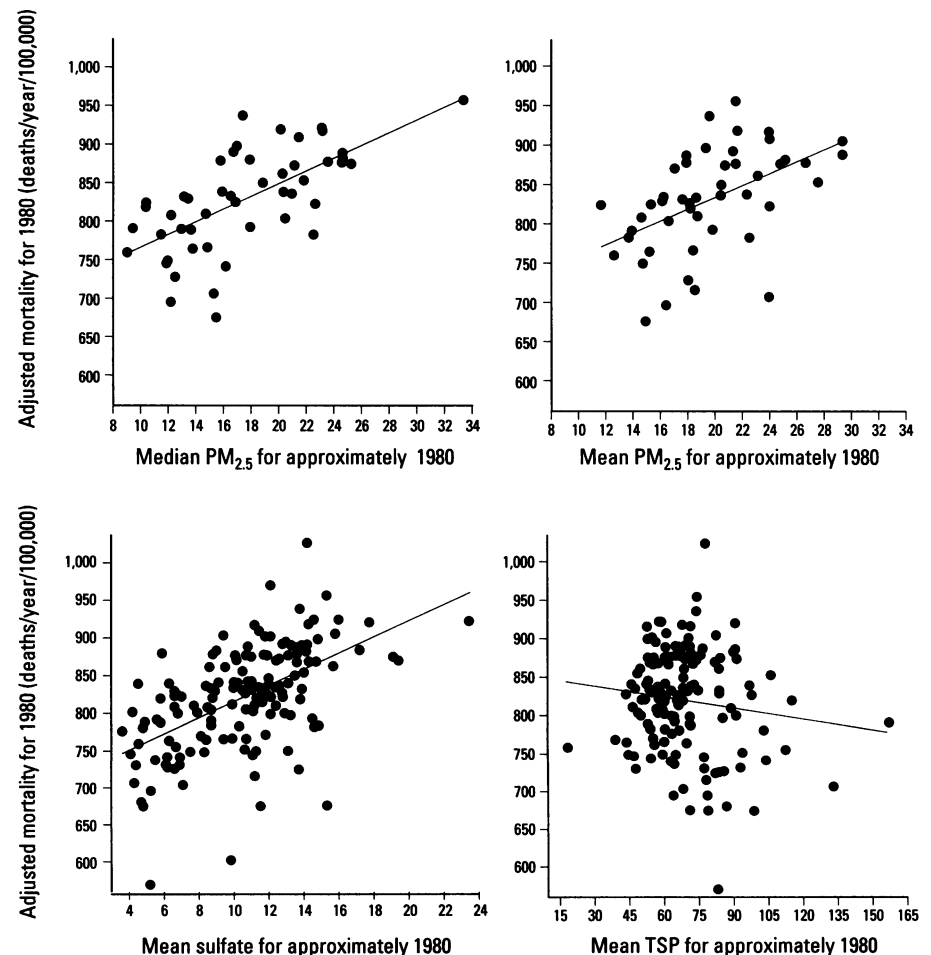
Figure 1. Age-, sex-, and race-adjusted population-based mortality rates in U.S. cities for 1980 plotted over various indices of particulate air pollution.

Table 4. Comparisons of mortality risk ratios (and 95% confidence interval) for air pollution from the Harvard Six-Cities, ACS, and postneonatal infant mortality studies.

| | Particulate air pollution (range of pollution) | | | | | |
Cause of death	Six-Cities (18.6 µg/m³ PM$_{2.5}$)	ACS (24.5 µg/m³ PM$_{2.5}$)	ACS (19.9 µg/m³ SO$_4$)	Infant (56.9 µg/m³ PM$_{10}$)	AHSMOG (males) (24.1 µg/m³ PM$_{10}$)	AHSMOG (females) (24.1 µg/m³ PM$_{10}$)
All	1.26 (1.08–1.47)	1.17 (1.09–1.26)	1.15 (1.09–1.22)	1.25 (1.12–1.47)	1.11 (0.98–1.26)	0.94 (0.84–1.04)
Cardiopulmonary	1.37 (1.11–1.68)	1.31 (1.17–1.46)	1.26 (1.16–1.37)	—	1.10 (0.94–1.30)	0.92 (0.80–1.05)
Respiratory mentioned[a]	—	—	—	—	1.23 (0.94–1.61)	1.10 (0.86–1.40)
SIDS, NBW	—	—	—	1.91 (1.46–2.44)	—	—
Lung cancer	1.37 (0.81–2.31)	1.03 (0.80–1.33)	1.36 (1.11–1.66)	—	3.36 (1.57–7.19)	1.33 (0.60–2.96)
All others	1.01 (0.79–1.30)	1.07 (0.92–1.24)	1.01 (0.92–1.11)	1.00[b] (0.94–1.06)	—	—

Abbreviations: NBW, normal birth weight; PM, particulate matter; SIDS, sudden infant death syndrome.
[a]Any mention on the death certificate of nonmalignant respiratory disease as an underlying or contributing cause of death. [b]NBW.

mortality studies have severe limitations and have been discounted for several reasons. An overriding concern is that they cannot directly control for individual differences in other important risk factors including cigarette smoking.

Survival/Life Expectancy

Several cohort-based mortality studies have evaluated effects of long-term pollution exposure. The first of these studies, often referred to as the Harvard Six-Cities study (162), involved a 14- to 16-year prospective follow-up of more than 8,000 adults living in six U.S. cities. It controlled for individual differences in age, sex, cigarette smoking, education levels, body mass index, and other risk factors. Cardiopulmonary mortality was significantly associated with mean sulfate and fine particulate concentrations over the years of the study period.

A second study, referred to as the ACS study, linked individual risk factor data from the American Cancer Society, Cancer Prevention Study II (CPS-II) with national ambient air pollution data (163). The analysis used data for more than 500,000 persons who lived in up to 151 different U.S. metropolitan areas and who were followed prospectively from 1982 through 1989. It controlled for individual differences in age, sex, race, cigarette smoking, and other risk factors, and evaluated the association of adjusted mortality with two indices of long-term exposure to combustion-source particulate air pollution, mean sulfate, and median fine particles. Both indices of combustion-source particulate air pollution were associated with overall mortality and especially with cardiopulmonary mortality.

In both the Harvard Six-Cities study (162) and the ACS study (163), the positive association between combustion-related air pollution and cardiopulmonary mortality was dominated by cardiovascular disease deaths. However, because of concerns about cause-of-death cross-coding on the death certificates, respiratory and cardiovascular deaths were grouped together and analyzed as cardiopulmonary deaths.

A study of postneonatal infant mortality in the U.S.-linked National Center for Health Statistics birth and death records for infants born between 1989 and 1991 with PM$_{10}$ data from the U.S. EPA's Aerometric Database (164). The full data set included approximately four million infants in 86 U.S. metropolitan areas. Because all infants in the study had PM$_{10}$ exposure for at least part of 2 months, the analysis compared postneonatal infant mortality across different levels of ambient PM$_{10}$ concentrations during the 2 months following birth. The analysis controlled for individual differences in maternal race, maternal education, marital status, month of birth, maternal smoking during pregnancy, and ambient temperatures. Particulate pollution exposure was associated with postneonatal infant mortality for all causes, respiratory causes, and sudden infant death syndrome.

A final cohort study, known as the Adventist Health Study of Smog (AHSMOG), related air pollution to 1977–1992 mortality in more than 6,000 nonsmoking adults living in California, predominantly from the three metropolitan areas of San Diego, Los Angeles, and San Francisco (161). All natural cause mortalities, nonmalignant respiratory mortalities, and lung cancer mortalities were significantly associated with ambient PM$_{10}$ concentrations in males, but not in females. Cardiopulmonary disease mortality was not significantly associated with PM$_{10}$ in either males or females. Unfortunately, this study did not have direct measures of PM$_{2.5}$ but relied on TSP and PM$_{10}$ data. Furthermore, the cohort was relatively small and was predominantly from only three metropolitan areas, San Diego, Los Angeles, and San Francisco.

Comparisons of mortality risk ratios for air pollution from the Six-Cities, ACS, infant mortality, and AHSMOG studies are presented in Table 4. The estimated overall excess risk from the infant mortality study is similar to those estimated for adults in the Harvard Six-Cities and ACS studies, even though the time frame of exposure for the

infants was clearly far shorter than for the adults. This observation suggests that the relevant time frame of exposure is short (a few months vs years) and/or that infants are at greater risk for exposure to air pollution.

Disease/Lung Function

There have also been several studies evaluating associations between chronic exposure and particulate air pollution and respiratory symptoms and disease or lung function (Table 3). The effects of air pollution on respiratory disease or symptoms were often estimated while adjusting for individual differences in various other risk factors. Significant associations between particulate air pollution and various respiratory symptoms were often observed. Chronic cough, bronchitis, and chest illness (but not asthma) were associated with various measures of particulate air pollution. Studies that evaluated effects of air pollution on lung function adjusted for individual differences in age, race, sex, height, and weight, and controlled for smoking or restricted the analysis to never-smokers. These studies observed small associations between decreased lung function and particulate air pollution that were often statistically significant.

Stylized Summary of Effects

The overall epidemiologic evidence is enhanced if adverse effects of exposure are reproducibly observed by different investigators in different settings. That is, there should be consistency of effects across independent studies. The evidence is further strengthened by a coherence of effects observed across a cascade of related health outcomes. Figure 2 presents a stylized summary of effect estimates of exposure to particulate air pollution. The effect estimates are not precise because different studies used various measures of pollution, different models, and differently defined health end points. In addition, the recent rapid growth of the literature in this area makes effect estimates a moving target. Figure 2, therefore, should be considered stylized but illustrative. The estimates for the

acute time-series studies are revised from recent reviews (6,8). The effect estimates for the cross-sectional and cohort studies are based on selected studies that are reasonably representative. The population-based mortality estimate is based on results presented by Evans et al. (155), Lipfert (157), Lipfert et al. (158), and Ozkaynak and Thurston (160). The cohort-based mortality estimates are based on Dockery et al. (162), Pope et al. (163), and Woodruff et al. (164), respectively. Bronchitis, children's lung function, and adult lung function estimates are based on results reported by Dockery et al. (167), Raizenne et al. (173), and Ackermann-Liebrich et al. (171), respectively.

As illustrated in Figure 2, a remarkable cascade of cardiopulmonary health end points has been observed. These include death from cardiac and pulmonary disease, emergency room and physician office visits for asthma and other cardiorespiratory disorders, hospital admissions for cardiopulmonary disease, increased reported respiratory symptoms, and decreased measured lung function. The overall epidemiologic evidence indicates a probable link between fine particulate air pollution and adverse effects on cardiopulmonary health. Nevertheless, there remains uncertainty about the role of chemistry versus size of the particles, the role of copollutants, and the use of central-site air quality monitoring to estimate the effects on individuals who spend most of their time indoors. In addition, there remains substantial uncertainty with regard to the biologic plausibility of these associations.

What Are the Biologic Mechanisms?

Our knowledge about the underlying biologic mechanisms remains limited and requires much additional study. The results of the epidemiology outlined above, however, provide a pattern of effects that may be biologically germane. Biologic plausibility is enhanced by the observation of a coherent cascade of cardiopulmonary health effects and by the fact that noncardiopulmonary health end points are not typically associated with the pollution. In addition, as summarized in Table 5, very recent epidemiologic studies have attempted to look at specific physiologic end points, in addition to lung function, that may be part of the pathophysiologic pathway linking cardiopulmonary mortality and particulate air pollution.

One hypothesized general pathway includes pollution-induced lung damage (potentially including oxidative lung damage and inflammation), declines in lung function, respiratory distress, and cardiovascular disease potentially related to hypoxemia (177). Evidence of pollution-related inflammation
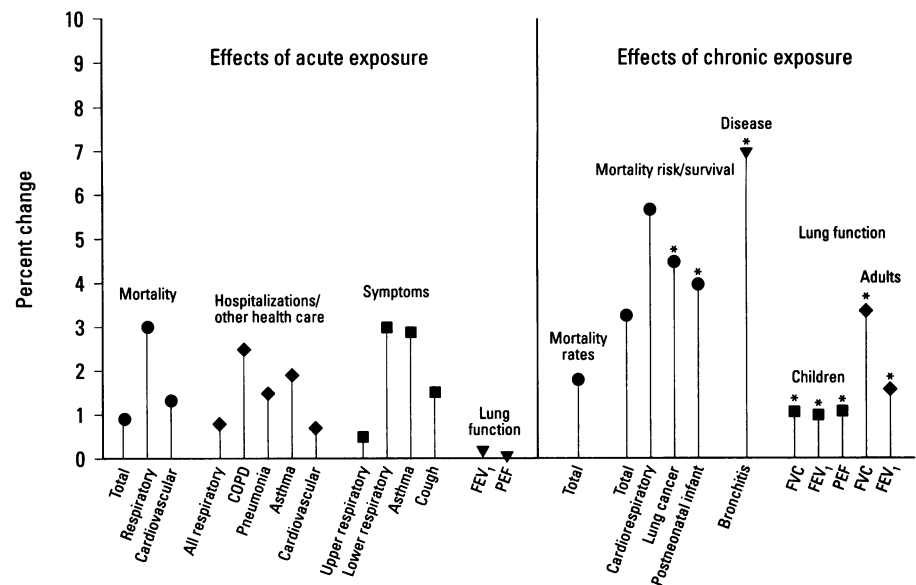

Figure 2. Stylized summary of observed health effects, presented as approximate percent changes in health end points per 5 µg/m³ increase in PM2.5. Abbreviations: COPD, chronic obstructive pulmonary disease; FVC, forced vital capacity; PEF, peak expiratory flow. Asterisk (*) indicates estimate based on very limited or inconsistent evidence.

Table 5. Brief summary of several recent epidemiologic studies of specific physiologic end points.

Physiologic end points	Observed associations with elevated particulate matter exposure	Authors/year (reference)
Lung function	Small declines in lung function; large risk of substantial decrements	Hoek et al. 1999 (125)
Hypoxemia	No clear associations with blood oxygen saturation	Pope et al. 1999 (177)
Plasma viscosity	Increased risk of elevated blood plasma viscosity	Peters et al. 1997 (178)
Heart rate	Increased mean HR and odds of a substantially elevated HR.	Pope et al. 1999 (177) Peters et al.1999 (179)
Heart rate variability	Changes in cardiac rhythm. Decrease in overall HRV.	Liao et al. 1999 (180) Pope et al. 1999 (181) Gold et al. 2000 (182)
Pulmonary inflammation	Elevated white blood cell counts, band cells expressed as percentage of polymorphonuclear leukocytes, platelets, lymphocytes, and eosinophils	Tan et al. 2000 (183) Salvi et al. 1999 (184)[a]

[a]This is actually a controlled human exposure study.

has been observed (183–185) and, as indicated above, several studies have reported declines in lung function associated with elevated particulate pollution exposures. However, a study of potential PM-related hypoxemia did not observe declines in blood oxygen saturation associated with elevated exposures to particulate air pollution (177).

Alternatively, the autonomic nervous system may play an important role in the pathophysiologic pathway between particulate exposure and cardiopulmonary disease. Seaton et al. (186) hypothesized that fine particulate air pollution may provoke alveolar inflammation, resulting in the release of potentially harmful cytokines and increased blood coagulability. Autonomic nervous system-activated changes in blood viscosity, heart rate (HR), and heart rate variability (HRV) may increase the likelihood of cardiac death (187). A few recent epidemiologic studies (177–183) have evaluated such autonomic nervous system-related physiologic

measures and air pollution, although they have been extremely limited and mostly exploratory pilot studies.

Peters et al. (178) evaluated blood plasma viscosity from a random sample of men and women living in Augsburg, Germany, during the winter of 1984–1985. Between January 4 and 7, 1985, there was a pollution episode with marked increases in sulfur oxide and particulate pollution concentrations. During this episode a significant increase in the risk of elevated plasma viscosity was observed. The odds ratios (and 95% confidence intervals [CIs]) for plasma viscosity were above the 95th percentile of the sample distribution; they were 3.6 (1.6–8.1) and 2.3 (1.0–5.3) for men and women, respectively.

A daily time-series panel study of elderly subjects with repeated measures of blood oxygenation did not observe pollution-related hypoxemia but did observe that elevated particulate air pollution levels were associated with increased pulse rate (177). A 100-mg/m³

increase in PM_{10} on the previous 1–5 days was associated with an average increase in the pulse rate of 0.8 beats/min and a 29% and 95% increase in the odds of the pulse rate being elevated by 5 or 10 beats/min, respectively.

In a related study (181), repeated 24-hr ambulatory electrocardiograph (ECG) monitoring was conducted on seven subjects for a total of 29 days during episodes of high pollution and during periods of relatively low pollution. HR was positively associated with particulate air pollution. Additionally, beat-to-beat (R-R) HRV was analyzed to assess cardiac autonomic control. Particulate air pollution was associated with changes in HRV including: reduced 24-hr SDNN (the standard deviation of all normal R-R intervals and an estimate of overall HRV); reduced SDANN (standard deviation of the averages of R-R intervals in all 5-min segments of the 24-hr ECG recording and an estimate of long-term components of HRV); and increased r-MSSD (the square root of the mean of squared differences between adjacent R-R intervals and an estimate of the short-term components of HRV). The associations between HRV and particulate pollution persisted even after controlling for mean HR, suggesting a possible link between elevated exposure to PM and lower cardiac autonomic control.

A prospective study of HRV and mortality in subjects with chronic heart failure was recently reported (187). Survival analysis conducted in this study included a Cox Proportional Hazards regression model to control for multiple risk factors. Based on this model the estimated risk ratio for a 41.2-ms decrease in SDNN (from 24-hr ambulatory ECG monitoring) was 1.62 (95% CI, 1.16–2.44). As an interesting but highly speculative look at plausibility, the 24-hr SDNN mortality relationship from this study can be combined with the decline in 24-hr SDNN associated with PM_{10} from the above HRV study (181). The expected increase in mortality risk can then be estimated and compared with the PM-related cardiovascular mortality risk directly estimated from the PM mortality epidemiology studies. For example, the estimated decline in 24-hr SDNN associated with 100 $\mu g/m^3$ PM_{10} was approximately 18 ms (SE = 4.9). Using the coefficients reported in these two studies (181,187), the estimated mortality risk ratio of an 18-ms decline in 24-hr SDNN can be calculated as 1.23 ($e^{[18*(\ln 1.62)/41.2]}$). This risk ratio seems somewhat plausible. It is larger than risk ratios for total or cardiovascular disease mortality that are generally estimated from daily time-series studies but smaller than risk ratios estimated from the prospective cohort mortality studies of long-term chronic exposure.

Two additional studies have also recently evaluated associations between particulate air pollution and HRV. One of these studies explored daily changes in HRV associated with daily changes in fine particulate air pollution with a panel of elderly subjects living in metropolitan Baltimore (180). Daily ECG monitoring was conducted with resting, supine, 6-min R-R interval data collected each day. The second study involved subjects 53–87 years of age living in Boston, Massachusetts (182). Weekly ECG monitoring was conducted using ambulatory (Holter) monitors continuously for 25 min, including 5 min of rest, 5 min of standing, 5 min of outdoor exercise, 5 min of recovery, and 20 cycles of slow breathing. Although the pollution levels were relatively low during the study periods in both of these studies, lower HRV was associated with elevated concentrations of fine particulate pollution, and the association was stronger for subjects with pre-existing cardiovascular conditions.

In the three currently available studies of particulate air pollution and HRV (180–182), a negative association with particulate exposure and overall HRV was observed. The results, however, are not entirely consistent, especially with measures of the short-term (or high-frequency) components of HRV. To what degree these inconsistencies across studies can be explained by differences in ECG monitoring time frames, make-up of subjects, differences in pollution levels, or other differences needs to be explored.

A study of rabbits found that alveolar macrophage phagocytosis of small carbon particles < 10 μm in aerodynamic diameter resulted in the release of cytokines that led to stimulation of the bone marrow to release young polymorphonuclear leukocytes (PMNs). The authors postulated that these PMNs caused the health effects noted in epidemiologic studies (188). A follow-up study was conducted of an air pollution episode due to fires in Southeast Asia in 1997 (183). Blood samples from 30 healthy male military personnel were collected during and after the episode. The pollution episode was associated with significant increases in total white blood cell counts, band cells expressed as a percentage of PMNs, platelets, lymphocytes, and eosinophils. The authors suggest that these results imply a systemic response to PM-related pulmonary inflammation. A recent controlled human study of exposure to diesel exhaust also observed a well-defined and marked systemic and pulmonary inflammatory response in healthy human volunteers (184).

The physiologic relevance of no PM-related hypoxemia but PM-related changes in blood plasma viscosity, HR, HRV, and pulmonary inflammation is not well understood.

Recent animal studies have observed somewhat complementary results (188–194), but the epidemiologic observations are preliminary and based on only a few studies, most of which were exploratory pilot studies. These changes may reflect PM-induced pulmonary inflammation, cytokine release, and altered cardiac autonomic function as part of the pathophysiologic mechanisms or pathways linking PM and cardiovascular mortality. In general, it is speculated that interactions between inflammation, abnormal hemostatic function, and altered cardiac rhythm may play an important role in the pathogenesis of cardiopulmonary diseases related to air pollution. An adequate understanding of these relationships clearly requires further research.

Who's at Risk?

The question of who is at risk or who is susceptible to adverse health effects of fine PM pollution does not have an easy answer. It seems evident that the elderly, young children, and persons with chronic cardiopulmonary disease, influenza, and asthma are most likely to be susceptible. However, this answer is far too simplistic. For example, assume a large population of nonsmokers. Require all in the population to smoke a pack of cigarettes for a day and then stop. Who will be susceptible to this relatively short-term exposure to cigarette smoking? Mortality and serious morbidity effects would most likely affect the very old, young, and those with asthma or chronic cardiopulmonary disease. This does not mean that others are unaffected. For healthy, middle-aged adults, the effects are unlikely to be immediately life threatening, but short-term adverse effects such as coughing, throat and eye irritation, or even mild or moderate cigarette smoke-induced pulmonary inflammation may be experienced. Further suppose smoking does not stop after 1 day but continues throughout the lives of all in the population. Now who is susceptible to exposure to cigarette smoke? Over a lifetime, the chronic exposure has the potential to eventually effect all. Although the exposures and effects for active cigarette smoking are much larger, cigarette smoking has been associated with a spectrum of cardiopulmonary diseases similar to those associated with fine PM. Interestingly, a decrease in HR and an increase in HRV have also been observed following smoking cessation (195). Clearly, the answer to the question of who is susceptible is not simple but is dependent on the health effects being evaluated and the level and length of exposure.

At Risk from Short-Term, Acute Exposure

A summary of who may be susceptible to various adverse health effects from PM

exposure and overall health relevance is presented in Table 6. With respect to acutely elevated exposures, reflected by day-to-day changes in PM, those susceptible to dying are the elderly, the very young, and persons with chronic cardiopulmonary disease, influenza, or asthma. During the London episode of 1952, for example, approximately 80–90% of the excess deaths were in adults with respiratory and/or cardiovascular disease that was generally chronic in nature. There was also an approximate doubling of deaths in children less than 1 year of age (20). As summarized in Table 2, more recent daily time-series studies also observe that most of the excess mortality from PM exposure is from respiratory and cardiovascular disease deaths.

How much life shortening is due to acutely elevated levels of PM and how much of the mortality is due to short-term mortality displacement (harvesting) remains uncertain. If the increased mortality is only in the most frail persons with little remaining life expectancy, then death may be advanced by only a few days or weeks. However, recent research using data from Philadelphia, Pennsylvania observed that the increase in mortality was inconsistent with only short-term mortality displacement and suggests that mortality for many may be substantially advanced (196). These results also suggest that those who are susceptible to increased risk of mortality from acutely elevated PM may include more than just the most old and frail who are already very near death.

On any given day, the number dying due to PM exposure is extremely small. Based on the 1996 average death rate for the United States (8.8/1000/year) and the summary estimates presented in Table 2, a 50-μg/m³ increase in $PM_{2.5}$ would result in an average of only 1.7 deaths per day per one million

people (compared to an expected rate of approximately 24/day). This minimal excess deaths per day reflects the fact that the increased risk of mortality due to acutely elevated PM exposure is small, and on any given day there may only be a very small fraction of the population at serious risk of dying due to this acute exposure.

As summarized in Table 6, the number of those susceptible to being hospitalized because of acute PM exposure is probably also quite limited and similar to the number of those at risk of dying. However, the number of those susceptible to less serious health effects such as increased respiratory symptoms, decreased lung function, or other physiologic changes may be quite broad. For most people, these effects are likely small, transient, and maybe even unnoticed. For a few, the decline in lung function may be clinically relevant (125), or the effects may be result in short-term absence from work (131,132) or school (141).

At Risk from Long-Term Chronic Exposure

Long-term, repeated PM exposure has been associated with increased population-based mortality rates (155–160) as well as increased risk of mortality in broad-based cohorts or samples of adults (162,163) and children (164) (Table 4). Chronic exposure studies of PM suggest rather broad susceptibility to cumulative effects of long-term repeated exposure. There is no evidence that increased mortality risk is unique to any well-defined susceptible subgroup. All who are chronically exposed may ultimately be affected. However, because the relative risk is small, the long-term cumulative effects are most likely to be observed in older age groups with relatively higher baseline risks of mortality.

To illustrate the potential cumulative mortality effects of PM, survival curves and life expectancies have been estimated under six different scenarios illustrated in Figure 3. The first curve is a baseline survival curve based on projected U.S. life tables prepared by the Office of the Chief Actuary in the Social Security Administration and obtained from the Berkeley Mortality Database (197). Although a survival curve for never-smokers and for persons not exposed to urban air pollution was not directly calculated, this projected baseline curve is used to represent a reasonable baseline estimate for the total U.S. population. The life expectancy of this baseline curve is equal to 76.4 years.

The second, third, and fourth survival curves are calculated from the baseline curve assuming an additional relative risk of mortality from PM exposure equal to 1.25. This is approximately the relative risk estimated in both the Harvard Six-Cities study (162) and the postneonatal infant mortality study (164) for the relevant range of PM air pollution that exists in U.S. urban areas (Table 4). The only difference between the second, third, and fourth curves is the age at which people begin to be susceptible to the effects of pollution. Curves two, three, and four assume that susceptibility begins at age 45 years, age 1 year, and at birth, respectively. As can be seen in Figure 3, these three survival curves appear to be nearly identical. The close concurrence between these three curves is because the baseline mortality risk for infants, children, and young adults is so low compared to the baseline mortality risks for older adults. The estimated life expectancy for curves two, three, and four equal 73.9, 73.5, and 73.4 years, respectively. This suggests an average loss of life expectancy equal to 2.5, 2.9, and 3.1 years, respectively. Obviously, earlier onset ages of susceptibility result in greater

Table 6. Summary of who's susceptible to adverse health effects from PM exposure and overall health relevance.

| Health effects	Who's susceptible?	Overall health relevance
Acute exposure		
Mortality	Elderly, infants, persons with chronic cardiopulmonary disease, influenza, or asthma	Obviously relevant. How much life shortening is involved and how much is due to short-term mortality displacement (harvesting) is uncertain.
Hospitalization/ other health care visits	Elderly, infants, persons with chronic cardiopulmonary disease, pneumonia, influenza, or asthma	Reflects substantive health impacts in terms of illness, discomfort, treatment costs, work or school time lost, etc.
Increased respiratory symptoms	Most consistently observed in people with asthma and children	Mostly transient effects with minimal overall health consequence, although for a few there may be short-term absence from work or school due to illness.
Decreased lung function	Observed in both children and adults	For most, effects seem to be small and transient. For a few, lung function losses may be clinically relevant.
Plasma viscosity, heart rate, heart rate variability, pulmonary inflammation	Observed in both healthy and unhealthy adults. No studies of children	Effects seem to be small and transient. Overall health relevance is unclear, but may be part of pathophysiologic pathway linking PM with cardiopulmonary mortality.
Chronic exposure		
Increased mortality rates, reduced survival times, chronic cardiopulmonary disease, reduced lung function	Observed in broad-based cohorts or samples of adults and children (including infants). All chronically exposed potentially are affected	Long-term, repeated exposure appears to increase the risk of cardiopulmonary disease and mortality. May result in lower lung function. Population average loss of life expectancy in highly polluted cities may be as much as a few years.
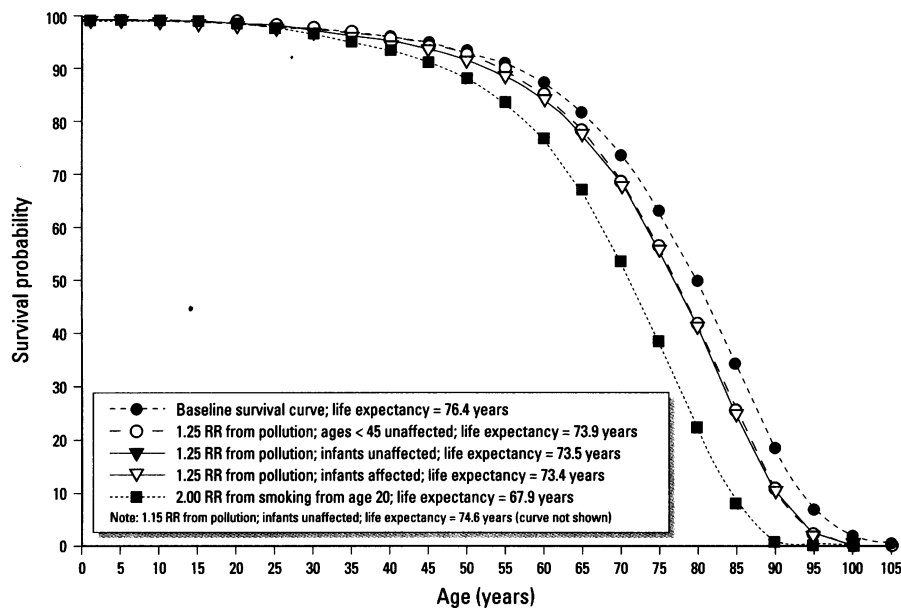
Figure 3. Survival curves based on projected U.S. life tables and alternative excess risk assumptions. Abbreviation: RR, relative risk.

overall loss of life. Differences in assumptions about the age when susceptibility begins, however, make only small differences for the younger ages because of the relatively low baseline mortality risks.

Survival curve five in Figure 3 was calculated from the baseline curve assuming an additional relative risk of mortality from cigarette smoking from age 20 equal to 2.00. This is approximately the average relative risk of approximately average levels of smoking versus never smoking that was estimated in both the Harvard Six-Cities study (*162*) and the ACS study (*163*). The estimated average life expectancy for smokers was 67.9, a loss of life expectancy equal to 8.6 years. Clearly, cigarette smoking has a much larger impact on mortality than ambient air pollution. However, this estimate of loss of life expectancy is not a population average, but the average loss to smokers only.

The sixth curve was calculated from the baseline curve assuming an additional relative risk of mortality from PM exposure equal to only 1.15. This is approximately the relative risk that was estimated from the ACS study (*163*) for the relevant range of PM air pollution in the United States (Table 4). Susceptibility was assumed to begin after infancy at age 1 year. The estimated life expectancy was 74.6, a loss of life expectancy equal to 1.8 years. These results are comparable to those obtained from two similar analyses (*198,199*).

Although the elevated risk associated with particulate air pollution exposure is relatively small compared with cigarette smoking, the public health significance of fine particulate air pollution, at least as measured in population

average loss of life, is substantial for two basic reasons. Exposure is ubiquitous. Because fine particles are often generated indoors and ambient fine particles penetrate many indoor environments, essentially everyone is exposed. Furthermore, exposure is not a voluntary decision made as a teenager or in adulthood but occurs throughout life.

The above estimates of population average life lost from the pollution are probably a worst-case scenario for the United States. They use relatively large estimates of excess risk from chronic exposure to pollution from the recent prospective cohort studies of adults and the postneonatal infant mortality study. They assume that the risk effects are cumulative for all or a large part of persons' lives, and they assume lifelong residency in one of the most polluted U.S. cities. Loss of life estimates due to pollution exposure of 1–3 years for lifelong residents of highly polluted cities, however, is not unreasonable, especially in some of the more polluted cities in the world.

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Human health effects of air pollution

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The effect of air pollutants on human health and underlying mechanisms of cellular action are discussed.

Abstract

Hazardous chemicals escape to the environment by a number of natural and/or anthropogenic activities and may cause adverse effects on human health and the environment. Increased combustion of fossil fuels in the last century is responsible for the progressive change in the atmospheric composition. Air pollutants, such as carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NOx), volatile organic compounds (VOCs), ozone (O_3), heavy metals, and respirable particulate matter (PM2.5 and PM10), differ in their chemical composition, reaction properties, emission, time of disintegration and ability to diffuse in long or short distances. Air pollution has both acute and chronic effects on human health, affecting a number of different systems and organs. It ranges from minor upper respiratory irritation to chronic respiratory and heart disease, lung cancer, acute respiratory infections in children and chronic bronchitis in adults, aggravating pre-existing heart and lung disease, or asthmatic attacks. In addition, short- and long-term exposures have also been linked with premature mortality and reduced life expectancy. These effects of air pollutants on human health and their mechanism of action are briefly discussed.
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Keywords: Air pollutant; Human health; Cellular actions; Detoxification

1. Introduction

Although a number of physical activities (volcanoes, fire, etc.) may release different pollutants in the environment, anthropogenic activities are the major cause of environmental air pollution. Hazardous chemicals can escape to the environment by accident, but a number of air pollutants are released from industrial facilities and other activities and may cause adverse effects on human health and the environment. By definition, an *air pollutant* is any substance which may harm humans, animals, vegetation or material. As far as humans are concerned an air pollutant may cause or contribute to an increase in mortality or serious illness or may pose a present or potential hazard to human health. The determination of whether or not a substance poses a health risk to humans is based on clinical, epidemiological, and/or animal studies which demonstrate that exposure to a substance is associated with health effects. In the context of human health, ''risk'' is the probability that a noxious health effects may occur.

2. Pollutant categories

The main change in the atmospheric composition is primarily due to the combustion of fossil fuels, used for the generation of energy and transportation. Variant air pollutants have been reported, differing in their chemical composition, reaction properties, emission, persistence in the environment, ability to be transported in long or short distances and their eventual impacts on human and/or animal health. However, they share some similarities and they can be grouped to four categories:

1. Gaseous pollutants (e.g. SO_2, NOx, CO, ozone, Volatile Organic Compounds).

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2. Persistent organic pollutants (e.g. dioxins).
3. Heavy metals (e.g. lead, mercury).
4. Particulate Matter.

Gaseous pollutants contribute to a great extent in composition variations of the atmosphere and are mainly due to combustion of fossil fuels (Katsouyanni, 2003). Nitrogen oxides are emitted as NO which rapidly reacts with ozone or radicals in the atmosphere forming NO_2. The main anthropogenic sources are mobile and stationary combustion sources. Moreover, ozone in the lower atmospheric layers is formed by a series of reactions involving NO_2 and volatile organic compounds, a process initiated by sun light. CO, on the other hand, is a product of incomplete combustion. Its major source is road transport too. While the anthropogenic SO_2 results from the combustion of sulphur-containing fossil fuels (principally coal and heavy oils) and the smelting of sulphur containing ores, volcanoes and oceans are its major natural sources. The latter contribute only ~2% of the total emissions. Finally a major class of compounds that fuel combustion and especially combustion processes for energy production and road transport are the major source of emission are the so called volatile organic compounds (VOCs). This is a class of compounds, which includes chemical species of organic nature such as benzene. Even though the majority of gaseous pollutants are inhaled and mainly affect the respiratory system they can also induce haematological problems (CO, benzene) and cancer.

Persistent organic pollutants form a toxic group of chemicals. They persist in the environment for long periods of time, and their effects are magnified as they move up through the food chain (bio-magnification). They include pesticides, as well as dioxins, furans and PCBs. Generally, the generic term ''dioxins'' is used to cover polychlorinated dibenzo-dioxins (PCDDs) and polychlorinated dibenzo-furans (PCDFs) while polychlorinated biphenyls (PCB) are called ''dioxin like compounds'' and can act similarly in terms of dioxin-type toxicity (Schecter et al., 2006). Dioxins are formed during incomplete combustion and whenever materials containing chlorine (e.g. plastics) are burned. Emitted in the atmosphere, dioxins tend to deposit on soil and water but, being water-insoluble, they do not contaminate ground water sources. Most dioxins in plants come from air and dust or pesticides and enter the food chain where they bio-accumulate due to their ability to be stably bound to lipids.

Heavy metals include basic metal elements such as lead, mercury, cadmium silver nickel, vanadium, chromium and manganese. They are natural components of the earth's crust; they cannot be degraded or destroyed, and can be transported by air, and enter water and human food supply. In addition, they enter the environment through a wide variety of sources, including combustion, waste water discharges and manufacturing facilities. To a small extent they enter human bodies where, as trace elements, they are essential to maintain the normal metabolic reactions. However, at higher (although relatively low) concentrations they can become toxic (Jarup, 2003). Most heavy metals are dangerous because they tend

to bio-accumulate in the human body. *Bioaccumulation* means an increase in the concentration of a chemical in a biological organism over time, compared to the chemical's concentration in the environment. Compounds accumulate in organisms any time they are taken in and stored faster than they are broken down (metabolized) or excreted.

Particulate matter (PM) is the generic term used for a type of air pollutants, consisting of complex and varying mixtures of particles suspended in the breathing air, which vary in size and composition, and are produced by a wide variety of natural and anthropogenic activities (Poschl, 2005). Major sources of particulate pollution are factories, power plants, refuse incinerators, motor vehicles, construction activity, fires, and natural windblown dust. The size of the particles varies ($PM_{2.5}$ and PM_{10} for aerodynamic diameter smaller than 2.5 μm and 10 μm respectively) and different categories have been defined: *Ultrafine* particles, smaller than 0.1 μm in aerodynamic diameter, *Fine* particles, smaller than 1 μm, and *Coarse* particles, larger than 1 μm. The size of the particles determines the site in the respiratory tract that they will deposit: PM_{10} particles deposit mainly in the upper respiratory tract while fine and ultra fine particles are able to reach lung alveoli. So far, no single component has been identified that could explain most of the PM effects. Among the parameters that play an important role for eliciting health effects are the *size and surface* of particles, their number and their composition. The composition of PM varies, as they can absorb and transfer a multitude of pollutants. However, their major components are metals, organic compounds, material of biologic origin, ions, reactive gases, and the particle carbon core. There is strong evidence to support that ultra fine and fine particles are more hazardous than larger ones (coarse particles), in terms of mortality and cardiovascular and respiratory effects. In addition, the metal content, the presence of PAHs and other organic components such as endotoxins, mainly contribute to PM toxicity.

3. Routes of exposure

Humans enter in contact with different air pollutants primarily via inhalation and ingestion, while dermal contact represents a minor route of exposure. Air pollution contributes, to a great extent, to the contamination of food and water, which makes ingestion in several cases the major route of pollutant intake (Thron, 1996). Via the gastrointestinal and respiratory tract, absorption of pollutants may occur, while a number of toxic substances can be found in the general circulation and deposit to different tissues. Elimination occurs to a certain degree by excretion (Madden and Fowler, 2000).

4. Health effects

Sporadic air pollution events, like the historic London fog in 1952 and a number of short and long term epidemiological studies investigated the effects of air quality changes on human health. A constant finding is that air pollutants contribute to increased mortality and hospital admissions (Brunekreef

and Holgate, 2002). The different composition of air pollutants, the dose and time of exposure and the fact that humans are usually exposed to pollutant mixtures than to single substances, can lead to diverse impacts on human health. Human health effects can range from nausea and difficulty in breathing or skin irritation, to cancer. They also include birth defects, serious developmental delays in children, and reduced activity of the immune system, leading to a number of diseases. Moreover, there exist several susceptibility factors such as age, nutritional status and predisposing conditions. Health effects can be distinguished to acute, chronic not including cancer and cancerous. Epidemiological and animal model data indicate that primarily affected systems are the cardiovascular and the respiratory system. However, the function of several other organs can be also influenced (Cohen et al., 2005; Huang and Ghio, 2006; Kunzli and Tager, 2005; Sharma and Agrawal, 2005).

4.1. Effects of air pollutants on different organs and systems

4.1.1. Respiratory system

Numerous studies describe that all types of air pollution, at high concentration, can affect the airways. Nevertheless, similar effects are also observed with long-term exposure to lower pollutant concentrations. Symptoms such as nose and throat irritation, followed by bronchoconstriction and dyspnoea, especially in asthmatic individuals, are usually experienced after exposure to increased levels of sulphur dioxide (Balmes et al., 1987), nitrogen oxides (Kagawa, 1985), and certain heavy metals such as arsenic, nickel or vanadium. In addition particulate matter that penetrates the alveolar epithelium (Ghio and Huang, 2004) and ozone initiate lung inflammation (Uysal and Schapira, 2003). In patients with lung lesions or lung diseases, pollutant-initiated inflammation will worsen their condition. Moreover air pollutants such as nitrogen oxides increase the susceptibility to respiratory infections (Chauhan et al., 1998). Finally chronic exposure to ozone and certain heavy metals reduces lung function (Rastogi et al., 1991; Tager et al., 2005), while the later are also responsible for asthma, emphysema, and even lung cancer (Kuo et al., 2006; Nawrot et al., 2006). Emphysema-like lesions have also been observed in mice exposed to nitrogen dioxide (Wegmann et al., 2005).

4.1.2. Cardiovascular system

Carbon monoxide binds to haemoglobin modifying its conformation and reduces its capacity to transfer oxygen (Badman and Jaffe, 1996). This reduced oxygen availability can affect the function of different organs (and especially high oxygen-consuming organs such as the brain and the heart), resulting in impaired concentration, slow reflexes, and confusion. Apart from lung inflammation, systemic inflammatory changes are induced by particulate matter, affecting equally blood coagulation (Riediker et al., 2004). Air pollution that induces lung irritation and changes in blood clotting can obstruct (cardiac) blood vessels, leading to angina or even to myocardial infraction

(Vermylen et al., 2005). Symptoms such as tachycardia, increased blood pressure and anaemia due to an inhibitory effect on haematopoiesis have been observed as a consequence of heavy metal pollution (specifically mercury, nickel and arsenic) (Huang and Ghio, 2006). Finally, epidemiologic studies have linked dioxin exposure to increased mortality caused by ischemic heart disease, while in mice, it was shown that heavy metals can also increase triglyceride levels (Dalton et al., 2001).

4.1.3. Nervous system

The nervous system is mainly affected by heavy metals (lead, mercury and arsenic) and dioxins. Neurotoxicity leading to neuropathies, with symptoms such as memory disturbances, sleep disorders, anger, fatigue, hand tremors, blurred vision, and slurred speech, have been observed after arsenic, lead and mercury exposure (Ewan and Pamphlett, 1996; Ratnaike, 2003). Especially, lead exposure causes injury to the dopamine system, glutamate system, and N-methyl-D-Aspartate (NMDA) receptor complex, which play an important role in memory functions (Lasley and Gilbert, 2000; Lasley et al., 2001). Mercury is also responsible for certain cases of neurological cancer. Dioxins decrease nerve conduction velocity and impaired mental development of children (Thomke et al., 1999; Walkowiak et al., 2001).

4.1.4. Urinary system

Heavy metals can induce kidney damage such as an initial tubular dysfunction evidenced by an increased excretion of low molecular weight proteins, which progresses to decreased glomerular filtration rate (GFR). In addition they increase the risk of stone formation or nephrocalcinosis (Damek-Poprawa and Sawicka-Kapusta, 2003; Jarup, 2003; Loghman-Adham, 1997) and renal cancer (Boffetta et al., 1993; Vamvakas et al., 1993).

4.1.5. Digestive system

Dioxins induce liver cell damage (Kimbrough et al., 1977), as indicated by an increase in levels of certain enzymes in the blood (see following discussion on the underlying cellular mechanisms of action), as well as gastrointestinal and liver cancer (Mandal, 2005).

4.2. Exposure during pregnancy

It is rather important to mention that air pollutants can also affect the developing foetus (Schell et al., 2006). Maternal exposure to heavy metals and especially to lead, increases the risks of spontaneous abortion and reduced fetal growth (preterm delivery, low birth weight). There are also evidences suggesting that parental lead exposure is also responsible for congenital malformations (Bellinger, 2005), and lesions of the developing nervous system, causing important impairment in newborn's motor and cognitive abilities (Garza et al., 2006). Similarly, dioxins were found to be transferred from the mother to the fetus via the placenta. They act as endocrine disruptors and affect growth and development of the central nervous

system of the foetus (Wang et al., 2004). In this respect, TCDD is considered as a developmental toxin in all species examined.

5. Cellular mechanisms involved in air pollutants actions

Common cellular mechanism by which most air pollutants exert their adverse effects is their ability to act directly as pro-oxidants of lipids and proteins or as free radicals generators, promoting oxidative stress and the induction of inflammatory responses (Menzel, 1994; Rahman and MacNee, 2000). Free radicals (reactive oxygen and nitrogen species) are harmful to cellular lipids, proteins, and nuclear- or mitochondrial-DNA, inhibiting their normal function (Valko et al., 2006). In addition, they can interfere with signaling pathways within cells (Valko et al., 2006). In eukaryotic aerobic organisms including humans, free radicals are continuously generated during normal metabolism and in response to exogenous environmental exposures (e.g. irradiation, cigarette smoke, metals and ozone). When free radical concentration increases, due to an overwhelming of organism's defense, a state of oxidative stress occurs. This oxidative state has been implicated in a wide variety of degenerative diseases such as atherosclerosis, heart attacks, stoke, chronic inflammatory diseases (rheumatoid arthritis), cataract, central nervous system disorders (Parkinson's, and Alzheimer's disease), age related disorders and finally cancer.

Furthermore, the toxic effects of heavy metals, apart from inducing oxidative stress, can be also attributed to their ability to substitute diverse polyvalent cations (calcium, zinc, and magnesium) that function as charge carriers, intermediaries in catalyzed reactions, or as structural elements in the maintenance of protein conformation. Indeed, metals accumulate in cellular organelles and interfere with their function. For example it has been observed that lead accumulation in mitochondria induces several changes such as inhibition of Ca^{2+} uptake, reduction of the transmembrane potential, oxidation of pyridine nucleotides, and a fast release of accumulated Ca^{2+} (Chavez et al., 1987). Moreover, metals bind to proteins

(Goering, 1993) and inhibit a large number of enzymes, including the mitochondrial ones (Rossi et al., 1993). Nucleic acid binding proteins are also involved, while it has been shown that metals can also bind to DNA, affecting the expression of genes. For example nickel enters the nucleus, interacts with chromatin and silences the expression of genes such as tumor suppressor genes, inducing carcinogenesis (Costa et al., 2003). Finally, some metals interfere with various voltage- and ligand-gated ionic channels exerting neurotoxic effects. For instance lead affects the *N*-methyl-D-aspartic acid (NMDA) receptor, subtypes of voltage- and calcium-gated potassium channels, cholinergic receptors and voltage-gated calcium channels (Garza et al., 2006; Toscano and Guilarte, 2005).

Dioxin causes a broad range of adverse effects (Birnbaum, 1994): they alter metabolism by inducing a number of metabolic enzymes (e.g. CYPs, glutathione-transferase, tyrosine kinase etc.), homeostasis, through hormone modulation (e.g. estrogens, androgens glucocorticoids, insulin, thyroid hormones) and their receptors, and growth and differentiation by interfering with growth factors (e.g. EGF, TGFα, TNFα) and their receptors. At the cellular level, dioxins interact with the aryl hydrocarbon receptor (AhR) (Schwarz et al., 2000) which has a basic helix-loop-helix domain, acting as a transcription factor after nuclear translocation, allowing interaction of dioxins with DNA. The receptor-ligand complex binds to specific sites on DNA, altering the expression of a number of genes.

As far as cancer is concerned from the data presented above it becomes clear that most pollutants play an important role in the initiation, promotion and progression of cancer cells (Fig. 1).

6. Natural protection

In our day-to-day life we are exposed in different kinds of pollutants. Health impacts, as already described above, depend on the pollutant type, its concentration, length of exposure, other coexisting pollutants and individual susceptibility.
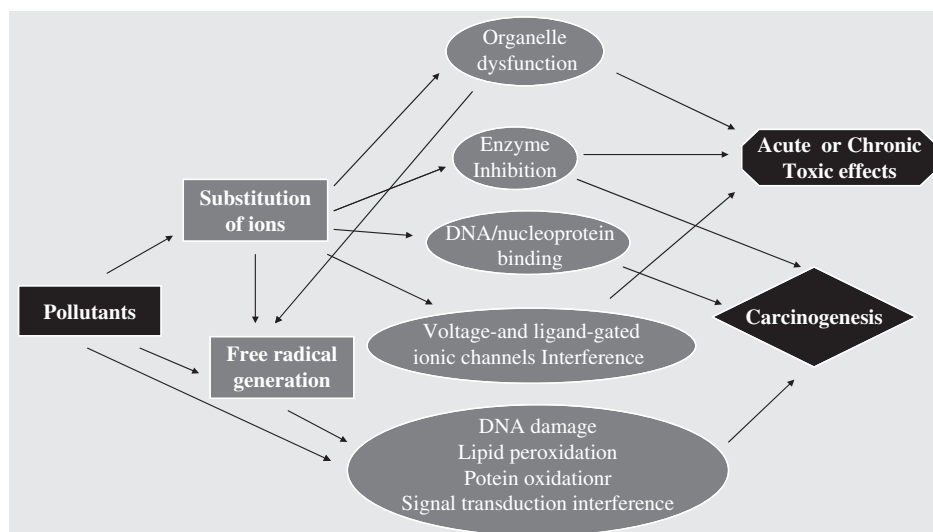

Fig. 1. Basic mechanisms of carcinogenesis.

People living in cities are exposed to a greater extent, as a consequence of increased industrialization and demands for energy and motor vehicles. Occupational exposure is also an important factor that should be taken into consideration. During the last decade, health effects of air pollution are studied more in developed countries, while more and better environmental monitoring data are required in order to setup threshold levels. In addition efforts should be intensified by taking the appropriate measures, in order to reduce the possibility of human pollutant exposure.

The human body, in order to protect itself against the potential harmful insults from the environment, is equipped with drug or xenobiotic metabolising enzymes (DMEs or XMEs) that play a central role in the biotransformation, metabolism and/or detoxification of xenobiotics or foreign compounds, including different kinds of pollutants. XMEs include a variety of enzymes such as cytochrome P450 (P450 or CYP), epoxide hydrolase, glutathione transferase, UDP-glucuronosyltransferase, sulfotransferase, NAD(P)H quinone oxidoreductase 1, and aldo-keto reductase. These enzymes mainly participate in the conversion of xenobiotics to more polar and water-soluble metabolites, which are readily excreted from the body. Finally, it should be noted that, in many cases, the chemically reactive metabolites produced during metabolism, are equally harmful and therefore undergo additional metabolism to inactive products. Hence, the final outcome of a compound modulating the detoxification enzyme systems is the result the effects on the different metabolic pathways.

A number of substances of dietary nature are beneficial, protective, and supportive of good health and the body's own natural chelation mechanisms. They include nutrients with natural chelating properties, which may help to detoxify the body, such as antioxidants, herbs, minerals, essential amino acids, other detoxifying or protective agents, and fiber (Kelly, 2004). Among them dietary antioxidants contribute to the organism's antioxidant defence system, that includes a series of antioxidant enzymatic (e.g. peroxidase) and non-enzymatic compounds (such as glutathione, or food-derived like vitamin E, or polyphenols), as well as damage removal/repair enzymes.

Several natural compounds, such as vitamins C, E, and A and polyphenols, found in the majority of plant foods, interfere with or scavenge ROS concentration within cells and subsequently protect the organism from the adverse effects of oxidative stress. Indeed, as it has been shown by our group that the antioxidant activity of plasma in humans following a diet rich in vegetables, fruits and olive oil was increased in comparison to a normal diet (Kampa et al., 2002). This increase can be mainly attributed to polyphenols which exhibit a wide range of biological activities, including anti-tumorigenic, anti-mutagenic, anti-inflammatory, and antiviral actions (Bravo, 1998; Hertog and Hollman, 1996) mainly due to their antioxidant properties and their ability to exert inhibitory effects by affecting basic cellular functions. Indeed the beneficial role of polyphenols in preventing cancer can be in part attributed to their ability to modify enzymes that activate or detoxify environmental carcinogens.

7. Conclusion

This brief review presents the adverse effects of a number of (air) pollutants in human health. As shown, major impairments of different organs can be observed. The main conclusion drawn is that, in view of increased exposure of humans in a diversity of pollutants, dietary interventions, rich in plant-derived foods, may protect or decrease their effects on different organs. This conclusion is supported by a number of epidemiological studies on the beneficial effect of a Mediterranean-type diet on human health.

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REVIEW ARTICLE

Clearing the Air: A Review of the Effects of Particulate Matter Air Pollution on Human Health

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Abstract The World Health Organization estimates that particulate matter (PM) air pollution contributes to approximately 800,000 premature deaths each year, ranking it the 13th leading cause of mortality worldwide. However, many studies show that the relationship is deeper and far more complicated than originally thought. PM is a portion of air pollution that is made up of extremely small particles and liquid droplets containing acids, organic chemicals, metals, and soil or dust particles. PM is categorized by size and continues to be the fraction of air pollution that is most reliably associated with human disease. PM is thought to contribute to cardiovascular and cerebrovascular disease by the mechanisms of systemic inflammation, direct and indirect coagulation activation, and direct translocation into systemic circulation. The data demonstrating PM's effect on the cardiovascular system are strong. Populations subjected to long-term exposure to PM have a significantly higher cardiovascular incident and mortality rate. Short-term acute exposures subtly increase the rate of cardiovascular events within days of a pollution spike. The data are not as strong for PM's effects on cerebrovascular disease, though some data and similar mechanisms suggest a lesser result with smaller amplitude. Respiratory diseases are also exacerbated by exposure to PM. PM causes respiratory morbidity and mortality by creating oxidative stress and inflammation that leads to pulmonary anatomic and physiologic remodeling. The literature shows PM causes worsening respiratory symptoms, more frequent medication use, decreased lung function, recurrent health care utilization, and increased mortality. PM exposure has been shown to have a small but significant adverse effect on cardiovascular, respiratory, and to a lesser extent, cerebrovascular disease. These consistent results are shown by multiple studies with varying populations, protocols, and regions. The data demonstrate a dose-dependent relationship between PM and human disease, and that removal from a PM-rich environment decreases the prevalence of these diseases. While further study is needed to elucidate the effects of composition, chemistry, and the PM effect on susceptible populations, the preponderance of data shows that PM exposure causes a small but significant increase in human morbidity and mortality. Most sources agree on certain "common sense" recommendations, although there are lonely limited data to support them. Indoor PM exposure can be reduced by the usage of air conditioning and particulate filters, decreasing indoor combustion for heating and cooking, and smoking cessation. Susceptible populations, such as the elderly or asthmatics, may benefit from limiting their outdoor activity during peak traffic periods or poor air quality days. These simple changes may benefit individual patients in both short-term symptomatic control and long-term cardiovascular and respiratory complications.

Keywords Particulate matter · Air pollution · Cardiovascular · Respiratory · Public policy

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Introduction

While some correlation between poor air quality and human disease has been recognized since antiquity, the health effects of air pollution entered the world's consciousness in the twentieth century. In 1930, sulfur dioxide from local

factory emissions mixed with a dense fog over the Meuse Valley in Belgium. Over 3 days, several thousand people were stricken with acute pulmonary symptoms, and 60 people died of respiratory causes [1]. In December 1952, a dense smog containing sulfur dioxide and smoke particulate descended upon London, resulting in more than 3,000 excess deaths over 3 weeks and as many as 12,000 through February 1953 [2]. The lethality of air pollution was immediately recognized but not well understood. To this day, because the effects of air pollution on illness occur at a population level, many clinicians fail to appreciate the relationship between air pollution and health.

The 1970 Clean Air Act (CAA) was the first major American regulatory effort aimed at both studying and setting limits on emissions and air pollution. The 1970 CAA defined the National Ambient Air Quality Standards (NAAQS [3]). These standards set limits on six primary pollutants found in air: carbon monoxide, lead, nitrogen dioxide, ozone, sulfur dioxide, and particulate matter (PM) [4].

PM is a complex mixture of extremely small particles and liquid droplets made up of acids, organic chemicals, metals, and soil or dust particles [5]. Sources of PM are both natural and anthropogenic. Manmade sources of PM include combustion in mechanical and industrial processes, vehicle emissions, and tobacco smoke. Natural sources include volcanoes, fires, dust storms, and aerosolized sea salt.

PM can be described by its "aerodynamic equivalent diameter" (AED). Particles of the same AED will tend to have the same settling velocity. Researchers traditionally subdivide particles into AED fractions based on how the particles are generated and where they deposit in human airways: <10, <2.5, and <0.1 μm (PM_{10}, $PM_{2.5}$, and $PM_{0.1}$, respectively). Particles with a diameter greater than 10 μm have a relatively small suspension half-life and are largely filtered out by the nose and upper airway. Researchers define a diameter between 2.5 and 10 μm ($PM_{2.5-10}$) as "coarse," less than 2.5 μm as "fine," and less than 0.1 μm as "ultrafine" particles. When interpreting PM research, it is important to appreciate that PM_{10} contains ultrafine ($PM_{0.1}$), fine ($PM_{0.1-2.5}$), and coarse ($PM_{2.5-10}$) fractions. In a mixed environmental sample, the total number and total surface area of these particles *increases* exponentially as the diameter of the particle decreases. However, the total particulate mass of a substance generally *decreases* exponentially with decreasing particle diameter. For example, in a sample of PM_{10}, the numerical majority of particles would be ultrafine, but these particles would make up a negligible portion of the sample's total particulate mass (Fig. 1).

Studies show an increase in morbidity and mortality related to PM exposure. While the increased daily risks from PM exposure are modest for any individual, the costs of the worldwide healthcare burden are staggering when applied to populations. The World Health Organization estimates that
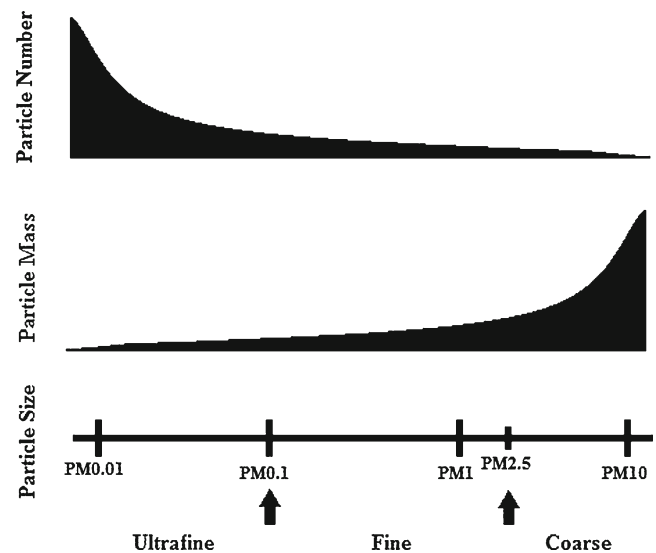

Fig. 1 A hypothetical mixed particle distribution

$PM_{2.5}$ concentration contributes to approximately 800,000 premature deaths per year, ranking it the 13th leading cause of mortality worldwide [6].

This paper provides a review of the effect of ambient airborne PM on human morbidity and mortality. We review the current understanding of the mechanisms that underlie the observed clinical findings. Emphasis is placed primarily on research concerning the cardiovascular, respiratory, and cerebrovascular systems. This review concludes with public health recommendations based on a summary of the reported literature's findings.

Methods

The authors conducted a scientific review of all available literature published over the last 30 years. Our primary objective was to determine the association or lack of association between PM and human health. Our secondary objective was to summarize the proposed mechanisms for any purported associations based on existing human, animal, and in vitro studies. We initiated a PubMed database search using the MESH terms "PM," "particulate matter," "air pollution," "ultrafine particles," "fine particles," "coarse particles," "PM10," "PM2.5," and "PM0.1." Articles were selected and agreed upon by the authors based on relevance and impact. Effort was made to provide both positive and negative studies where appropriate. Emphasis was placed on well-conducted trials and epidemiological investigations. Studies were only excluded for redundancy. After analysis of the available data, this paper concludes with individual and public health recommendations based on the existing scientific evidence.

PM and Cardiovascular Health Effects

Several large studies suggest that PM exerts significant effects on the cardiovascular system [7–9]. Research on this topic has focused on both the long-term effects of chronic PM exposure and the acute effects of increases in ambient PM on cardiovascular mortality. In a previous analysis [10], it was shown that for any increase in mortality caused by PM, two thirds of the effect was accounted for by the cardiovascular diseases.

Cardiovascular Mechanisms

Animal studies demonstrate a link between chronic PM exposure and the development of atherosclerosis via systemic inflammation [11, 12]. Human studies show that the effects appear to be mediated by the inflammatory cytokines IL-6, TNF-ά, and C-reactive protein (CRP). Increases in both IL-6 [13] and CRP [14] have been associated with the development of acute myocardial infarction. Ruckerl et al. [15] described transient IL-6 and TNF-ά elevations in diabetic patients for 2 days following PM10 exposure. In a prospective cohort study of German patients, Hoffman et al. [16] associated exposure to PM2.5 with elevations in CRP. Other researchers demonstrated similar increases in CRP from PM10 exposure from both combustion [17] and organic matter [18]. In contrast, some studies have found only a weak or absent link between PM and markers of inflammation [19–22]. Discrepancies among studies appear related to differences in composition of PM, variable exposure to anti-inflammatory medications, and differences in obtaining PM exposure data [10].

Acute exposure to PM causes changes in coagulation and platelet activation providing a more proximal link between PM and coronary artery disease. Many experts consider fibrinogen to be an important risk factor for cardiovascular disease [10]. Ruckerl et al. [15] associated a 5-day cumulative exposure to PM_{10} with increased fibrinogen levels in survivors of myocardial infarction. Other pro-coagulant factors, such as plasminogen activator fibrinogen inhibitor-1 (PAI-1),

were also associated with PM elevations [17]. Intratracheal instillation of diesel exhaust particles led to increased platelet activation in hamsters and rapid thrombosis formation [23]. Further hamster studies also suggested that small particles translocate into the blood stream and exert prothrombotic effects [24]. Schicker et al. [18] showed that transient increases in PM10 exposure caused during hay-stacking increased platelet aggregation within 2 h of the activity. This activity also increased Von Willebrand factor and Factor VIII, markers of vascular endothelial activation.

Long-Term Effects

The "Harvard Six Cities study [7]," a cohort study published in 1993, followed 8,111 patients for 16–18 years and showed a 29% (95% CI, 8–47%) increase in the adjusted mortality rate for the most polluted of the cities compared to the least polluted. Particulate air pollution was positively associated with death from lung cancer and cardiopulmonary disease (Table 1).

Pope et al. [8] followed this in 1995 with another prospective cohort study of 552,000 patients in 151 metropolitan areas using the American Cancer Society's Cancer Prevention 2 database (ACS CPS 2). These data showed a 17% (95% CI, 9–26%) increase in all-cause mortality and a 31% (95% CI, 17–46%) increase in cardiopulmonary mortality when comparing the most and least polluted cities. In 2002 [25] and 2004 [26], Pope et al. re-reviewed the expanding ACS CPS 2 database, now with 1.2 million participants, and extended the follow up. Their research demonstrated an average increase in cardiopulmonary mortality of 9% (95% CI, 3–16%) for each 10-μg/m^3 increase in PM$_{2.5}$. Subsequently, they determined that a 10-μg/m^3 increase in PM increased ischemic cardiovascular disease mortality by 18% (95% CI, 14–23%) and mortality from arrhythmia, congestive heart failure, and cardiac arrest by 13% (95% CI, 5–21%).

In 2007, the Women's Health Initiative Study [27] followed a cohort of over 65,000 postmenopausal women with no previous

Table 1 Long-term effects of PM on the cardiovascular system

Author	Year	PM	ΔPM (in μg/m^3)	Outcome measure	Effect (95% CI)
Dockery et al. [17]	1993	PM$_{10}$	18.6	All-cause mortality	26% (8–47)
Pope et al. [18]	1995	PM$_{10}$	24.5	All-cause mortality	17% (9–26)
		PM$_{10}$	24.5	Cardiopulmonary mortality	31% (17–46)
Hoek et al. [28]	2002	BS	10.3	Cardiopulmonary mortality	71% (10–167)
Pope et al. [25]	2002	PM$_{2.5}$	10	Cardiopulmonary mortality	9% (3–16)
Pope et al. [26]	2004	PM$_{2.5}$	10	Ischemic CVD mortality	18% (14–23)
		PM$_{2.5}$	10	CHF, arrhythmia, CP arrest	13% (5–21)
Miller et al. [27]	2007	PM$_{2.5}$	10	Cardiovascular event	24% (9–41)
		PM$_{2.5}$	10	Cardiovascular mortality	76% (25–147)
Toren et al. [29]	2007	PM	Not measured	Cardiovascular mortality	12% (7–19)

PM particulate matter, *ΔPM* increase in ambient PM, *BS* black smoke

heart disease over approximately 6 years. The investigators revealed that long-term PM exposure in this population resulted in a 24% (95% CI, 9–41%) increase in cardiovascular events and an astonishing 76% (95% CI, 25–147%) increase in cardiovascular mortality per 10-μg/m^3 increase in $PM_{2.5}$. While these results had fairly wide confidence intervals, these data suggest that this cohort of patients may be particularly susceptible to ambient PM exposure.

The findings of cardiovascular effects from PM exposure are not unique to the USA. In the Netherlands, long-term exposure to traffic-related air pollution increased cardiopulmonary mortality by 71% (95% CI, 10–167%) [28]. A 2007 cohort study [29] of 250,000 Swedish construction workers from 1972 to 2002 found that workers with occupational PM exposure had a 12% (95% CI, 7–19%) increase in ischemic cardiovascular disease mortality.

While increases in PM have been consistently shown to increase cardiovascular morbidity and mortality, the effects of PM reduction have also been studied. In the 72 months following the ban of bituminous coal sales in Ireland in 1990, black smoke concentration decreased by 35.6 μg/m^3 over this time, and standardized respiratory and cardiovascular mortality decreased by 15.5% (95% CI, 12–19%) and 10.3% (95% CI, 8–13%), respectively [30]. An 8-year extension of the Harvard Six Cities data studied the population subset that moved from areas of higher to lower PM concentration [31], finding that a 10-μg/m^3 decrease in $PM_{2.5}$ resulted in a 27% (95% CI, 5–43%) decrease in overall mortality.

Short-Term Effects

A 2001 review [32] of 12 prior studies concluded that a 10-μg/m^3 increase in PM_{10} increased hospital admissions for congestive heart failure and ischemic heart disease by 0.8% (95% CI,

0.5–1.2%) and 0.7% (95% CI, 0.4–1.0%), respectively. Similarly, a 2006 review [33] showed a 0.44% (95% CI, 0.02–0.86%) and 1.28% (95% CI, 0.78–1.78%) increase in admissions for ischemic heart disease and heart failure for a 10-μg/m^3 increase in $PM_{2.5}$, respectively. In a smaller trial, Pope et al. [34] used a case-crossover of 12,000 patients in Utah to show that a 10-μg/m^3 increase in $PM_{2.5}$ led to a 4.5% (95% CI, 1.1–8.0) increase in acute ischemic coronary events. In an analysis of PM concentrations from 20 major cities in the USA using the National Morbidity Mortality Air Pollution Study (NMMAPS) data, Samet et al. [9] showed a 10-μg/m^3 increase in PM_{10} caused an increase in all-cause and cardiopulmonary mortality by 0.5% (95% CI, 0.1–0.9%) and 0.7% (95% CI, 0.2–1.2%), respectively (Table 2).

Similar results have been found in Japan [35], Australia, and New Zealand [36]. In 2008, Samoli et al. [37] re-analyzed the data of the APHEA 2, NMMAPS, and several Canadian studies in order to assess the coherence of findings using the same methods for all three sets of data. They were able to show an increase in daily all-cause mortality for Canadian, European, and US cities. Interestingly, the short-term mortality resulting from acute increases in PM are not limited to the critically ill or dying. In fact, much of the mortality occurred among active individuals with one or more risk factors.

PM and Respiratory Health Effects

While much of the interest in PM has focused on the cardiovascular system [7, 8], many studies evaluated the association between PM exposure and respiratory illness. Researchers have evaluated endpoints including respiratory symptoms, medication use, lung function, health-care utilization, and mortality.

Table 2 Short-term effects of PM on the cardiovascular system

Author	Year	PM	ΔPM (in μg/m^3)	Outcome measure	Effect
Morris [32]	2001	PM_{10}	10	Hospital admission, IHD	0.7% (95% CI, 0.4–1.0)
		PM_{10}	10	Hospital admission, CHF	0.8% (95% CI, 0.5–1.2)
Domicini et al. [33]	2006	$PM_{2.5}$	10	Hospital admission, IHD	0.44% (95% CI, 0.02–0.86)
		$PM_{2.5}$	10	Hospital admission, CHF	1.28% (95% CI, 0.78–1.78)
Barnett et al. [36]	2006	$PM_{2.5}$	10	Hospital admission, IHD	1.6% (95% CI, 0.7–2.4)
		$PM_{2.5}$	10	Hospital admission, CHF	3.6% (95% CI, 1.8–5.4)
		$PM_{2.5}$	10	Hospital admission, AMI	2.7% (95% CI, 1.3–4.2)
Pope et al. [34]	2006	$PM_{2.5}$	10	Ischemic cardiac event	4.5% (95% CI, 1.1–8.0)
Samet et al. [9]	2000	PM_{10}	10	All-cause mortality	0.5% (95% CI, 0.1–0.9)
		PM_{10}	10	Cardiopulmonary mortality	0.7% (95% CI, 0.2–1.2)
Omori et al. [35]	2003	TSP	20	All-cause mortality	1.0% (95% CI, 0.8–1.3)
		TSP	20	Cardiopulmonary mortality	1.1% (95% CI, 0.7–1.5)

PM particulate matter, *ΔPM* increase in ambient PM, *TSP* total suspended particles, *IHD* ischemic heart disease, *CHF* congestive heart failure, *AMI* acute myocardial infarction

Respiratory Mechanisms

PM triggers pulmonary oxidative stress and inflammation. Human airway epithelial cells exposed to PM express inflammatory cytokines [38, 39]. Alveolar macrophages exhibit respiratory burst activity, producing reactive oxygen species, nitrogen species, and release TNF-ά and IL-1 after exposure [40]. In addition to oxidative stress generated from activation of inflammatory cells, reactive oxygen species may be directly generated from the surface of particles [41]. These responses can be potent and were shown to cause measurable pulmonary damage after only a single exposure in mice [42]. This oxidative damage is associated with the primary development of asthma and chronic obstructive pulmonary disease (COPD). Long-term exposure to PM results in airway remodeling and chronic inflammation [43]. PM may also contribute to asthma development by enhancing atopy and IgE responses [44, 45]. Several controlled human experiments have demonstrated adverse affects on the pulmonary system. PM exposure has been shown to increase airway responsiveness to methacholine [46], increase neutrophil numbers in bronchial lavage [47], decrease CO diffusion capacity, and decrease maximum mid-expiratory flow [48].

Respiratory Symptoms and Medication Usage

As part of the Children's Health Study, McConnell et al. [49] found that asthmatic children had a 40% (95% CI, 10–80%) increased risk of bronchitic symptoms for a 19-$\mu g/m^3$ increase in PM_{10}. Similarly, a 10-$\mu g/m^3$ increase in PM_{10} led to a 12% (95% CI, 4–22%) increase in severe asthma symptoms in Seattle children [50]. A study of inner-city asthmatic children revealed an association between $PM_{2.5}$ increases and missed school days for asthma [51]. A study of adult Parisians [52] showed a 41% (95% CI, 16–71%) increase in acute asthma exacerbations per 10-$\mu g/m^3$ increase in PM_{10}. Interestingly, nearly all PM levels in these studies were below levels set out in the NAAQS.

Respiratory medication use also increased in times of peak PM concentration. Use of rescue bronchodilators increased as ambient $PM_{2.5}$ rose in Denver [53] and the Northeast USA [54]. A review of 80,000 Alaskan Medicaid enrollees found prescription rates for bronchodilators increased by 18.1% and 28.8% when PM_{10} exceeded 34 and 61 $\mu g/m^3$, respectively [55]. Together, these data suggest that increases in ambient PM worsen asthma symptoms.

PM and Pulmonary Function

Several recent studies suggest that PM levels may affect lung function and lung development. The Children's Health Study [56] followed 1,759 patients over 8 years, finding that children who lived in communities with the highest PM concentrations were five times more likely to have low FEV1 than those in communities with the lowest PM concentrations. Moreover, children that moved from areas of higher to lower PM_{10} concentration had increased growth in lung function, and those that moved from areas of lower to higher PM_{10} concentration had decreased growth in lung function [57]. Even children with better lung function were susceptible to new onset asthma when exposed to higher levels of $PM_{2.5}$ [58]. Lower lung function has also been shown for children with cystic fibrosis exposed to higher levels of PM_{10} and $PM_{2.5}$ [59].

Similar inverse correlations between PM exposure and individual PEFR and FEV1 measurements have been reproduced internationally [60]. In the developing world, where indoor biomass burning can lead to PM levels exceeding 200 $\mu g/m^3$, researchers demonstrated that chronic exposure in children can lead to adult COPD, increased rates of lung infection, and impaired lung function [61].

In adults, effects of PM on lung function have been found primarily in susceptible populations. Investigators showed that asthmatic Londoners taking walks in areas of high PM had significantly higher reduction in FEV1, FVC, and increases in sputum biomarkers of inflammation [62]. In elderly patients, PM_{10} and $PM_{2.5}$ increases were associated with decreases in PEFR [63]. In COPD patients, decrements in lung function were associated with increases in $PM_{2.5}$ concentration [64]. Downs et al. [65] demonstrated that declines in PM_{10} concentration may actually lead to an attenuated decline in lung function in adult patients. However, research on healthy adults has not as consistently shown an association between PM and respiratory compromise [66].

PM and Respiratory-Related Healthcare Utilization

In a large case–control study [67], 10 $\mu g/m^3$ increases in $PM_{2.5}$ were associated with a 9% (95% CI, 4–14%) increase in bronchiolitis hospitalizations for infants. Large pediatric studies demonstrate increased asthma ED visits for increases in PM [68] and that PM_{10} increases of 6.5 $\mu g/m^3$ are associated with a 15% (95% CI, 2–30%) increase in respiratory-related hospital admissions [69] (Table 3).

For adults, several large studies have demonstrated an association between respiratory hospitalization and ambient PM_{10} [70] and $PM_{2.5}$ [71] concentrations. This includes admissions for asthma, COPD, and pneumonia. The effects appear to be stronger for elderly patients with even short-term exposures [72]. A study [73] of 12 million Medicare enrollees in 108 counties demonstrated significant increases in respiratory hospitalizations for increases in $PM_{2.5}$ in the Eastern USA. Because the same effects were not consistently observed in the Western USA, the authors suggested that morbidity may be related to the specific chemical constituents of PM which differs across the country. Several recent

Table 3 The effects of PM on respiratory admissions

Author	Year	PM	ΔPM (in μg/m³)	Outcome measure	Effect (95% CI)
Karr et al. [67]	2006	PM$_{2.5}$	10	Infant bronchiolitis admissions	9% (4–14)
Lin et al. [68]	2005	PM$_{10–2.5}$	6.5	Pediatric respiratory admissions	17% (6–29)
Samoli et al. [92]	2011	PM$_{10}$	10	Pediatric asthma admissions	2.54% (0.06–5.08)
Peng et al. [93]	2008	PM$_{10–2.5}$	10	Respiratory admissions	0.33% (−0.21–0.86)
Zanobetti et al. [70]	2009	PM$_{2.5}$	10	Respiratory admissions	2.07% (1.2–2.95)
		PM$_{2.5}$	17	Pneumonia admissions	6.5% (1.1–11.4)
Medina-Ramon et al. [71]	2006	PM$_{10}$	10	COPD admissions	1.47% (0.93–2.01)
		PM$_{10}$	10	Pneumonia admissions	0.84% (0.5–1.19)
Dominici et al. [33]	2006	PM$_{2.5}$	10	COPD admissions	1.61% (0.56–2.66)
McGowan et al. [77]	2001	PM$_{10}$	14.8	Respiratory admissions	3.37% (2.34–4.40)
Ostro et al. [94]	2009	PM$_{2.5}$	14.6	Pediatric respiratory admissions	4.1% (1.8–6.4)

PM particulate matter, *ΔPM* increase in ambient PM

large studies have provided further evidence that the strength of PM effect may depend on the composition [74]. Investigations in European cities [75], Asian cities [76], and Oceania cities [77] have demonstrated a consistent and small though significant association between PM concentrations and emergency visits for respiratory diseases.

PM and Respiratory Mortality

The Six Cities study [7], 20 cities study [9], and ACS CPS 2 [8] cohort revealed an association between PM exposure and cardiopulmonary mortality. These studies did not, however, separate the impact on respiratory mortality versus cardiovascular mortality. A follow-up investigation using data from the 20 Cities Study revealed a 0.87% (95% CI, 0.38–1.36%) increased respiratory mortality for short-term increases in PM$_{10}$ by 10 μg/m³ [78]. This was subsequently expanded into a larger cohort of 112 US cities, where researchers found a 1.68% (95% CI, 1.04–2.33%) increase in respiratory mortality for every 10-μg/m³ increase in PM$_{2.5}$ [79]. A study of California counties similarly revealed an increased respiratory mortality with increases in PM$_{10}$ [80].

These results have been reproduced in countries around the world. A Norwegian study [81] demonstrated a 17% (95% CI, 9–25%) increase in mortality risk from COPD for every quartile increase in PM$_{2.5}$. In a study of 275,000 adults in ten Italian cities [82], short-term PM$_{10}$ increases led to a 2.29% (95% CI, 1.03–3.58%) increase in respiratory mortality. Similar results for increased respiratory mortality have been found in Asian cities where researchers have demonstrated excess respiratory mortality risk for increases in PM$_{10}$ [83]. Nearly identical effect sizes for respiratory mortality were found in the APHEA2 trial which studied this relationship across 29 European cities [84]. One study even demonstrated an association between PM$_{10}$ and respiratory mortality in children under age five [85] (Table 4).

PM and Cerebrovascular Health Effects

Ischemic cerebrovascular and cardiovascular disease share many risk factors, features, and pathophysiological mechanisms. As an example, CRP, similar to cardiovascular disease, has also been implicated in the genesis of stroke [86].

Table 4 The effects of PM on respiratory mortality

Author	Year	PM	ΔPM (in μg/m³)	Outcome measure	Effect (95% CI)
Zeka et al. [78]	2005	PM$_{10}$	10	Respiratory mortality	0.87% (0.38–1.36)
Zanobetti et al. [79]	2009	PM$_{2.5}$	10	Respiratory mortality	1.68% (1.04–2.33)
Wong et al. [83]	2008	PM$_{10}$	10	Respiratory mortality	0.62% (0.22–1.02)
Analitis et al. [84]	2006	PM$_{10}$	10	Respiratory mortality	0.58% (0.21–0.95)
Hales et al. [91]	2010	PM$_{10}$	10	Respiratory mortality	1.3% (0.5–2.1)
Pope et al. [25]	2002	PM$_{2.5}$	10	Lung cancer mortality	8% (1–16)
Ostro et al. [80]	2006	PM$_{2.5}$	10	Respiratory mortality	2.2% (0.6–3.9)

PM particulate matter, *ΔPM* increase in ambient PM

However, the evidence linking PM and stroke is more sporadic and the mechanisms less well understood.

Dominici et al. [33] reviewed an air quality data for 204 US urban counties and showed that a 10-μg/m^3 increase in ambient PM$_{2.5}$ increased the risk of hospitalization for cerebrovascular events by 0.8% (95% CI, 0.3–1.3%). A separate review [87] of Medicare patients found an increase of 1.03% (95% CI, 0.04–2.04%) for hospital admission for ischemic stroke for each 10-μg/m^3 increase in PM$_{10}$. Still other investigators found a previous day PM$_{2.5}$ increase of 5.2 μg/m^3 led to a 3% (95% CI, 0–7%) increase in risk of TIA and ischemic stroke.

In contrast, a recent large prospective multi-center stroke registry found no increase in the general population for ischemic stroke from exposure to PM$_{2.5}$. There was, however, an 11% (95% CI, 1–22%) increase in stroke risk in exposed patients with diabetes [88]. A large case-crossover study found an association between other components of air pollution (NO2 and CO) and cerebrovascular disease, but no correlation was noted with changing PM levels [89]. Similarly, a large registry of first-ever strokes found no association with PM$_{10}$ for ischemic or hemorrhagic stroke [90].

There are several reasons why studies of PM and cerebrovascular disease have produced conflicting results. Some studies do not completely adjust for all confounding variables. There is further heterogeneity due to differences in the definition of cerebrovascular disease, or whether pollution is measured on the day of admission or symptom onset [88]. Further, it is possible that exposure to PM may not contribute to an overall increase in cerebrovascular disease, but only trigger events in vulnerable populations.

Recommendations and Conclusions

In evaluating the literature, there appears to be a small, but consistent and significant, effect of PM on human health. Overall, the small individual effects result in a large global public health burden. Notably, the effects are most pronounced for cardiovascular disease. Several studies have demonstrated an increase in cardiovascular mortality and hospitalizations. There are similar effects, of smaller amplitude, in respiratory disease. More study is needed to clarify the relationship between PM and cerebrovascular disease.

There are limitations to much of the available PM research. Most studies do not use individual exposure data. Rather, air monitors in population centers are used as surrogates for individual exposure. Even after adjusting these data for time spent in traffic, exposure to second-hand smoke, etc., estimates may not be accurate. Despite these limitations, different types of studies conducted in different locations find similar results. A dose–response relationship between PM exposure and adverse effects has been identified, and improvement in health endpoints is observed when the PM exposures are reduced. Overall, the available evidence suggests a causal association between long- and short-term PM exposure and cardiovascular and respiratory morbidity and mortality.

Further research is still needed to fully understand how PM affects human health. While studies show increased PM concentration has adverse health affects, the actual composition of particulates that is harmful has not yet been elucidated. Further studies are also needed to clarify the time course of PM-induced effects. In limited studies, some effects seem to appear within hours, while other reach their zenith within several days peak PM exposure. The data on this "lag time" effect can

Table 5 Air quality index and recommendations

AQI level	AQI value	PM$_{2.5}$	PM$_{10}$	Actions to protect your health from particle pollution
Good	0–50	0–15	0–50	None
Moderate	51–100	16–35	51–154	Unusually sensitive people should consider reducing prolonged or heavy exertion
Unhealthy for sensitive groups	101–150	36–65	155–254	Susceptible groups[a] should reduce prolonged or heavy exertion
				Everyone else should limit prolonged or heavy exertion
Unhealthy for sensitive groups	151–200	66–150	255–354	Susceptible groups[a] should avoid all physical activity outdoors
				Everyone else should avoid prolonged or heavy exertion
Very unhealthy	201–300	>150	>354	Susceptible groups[a] should remain indoors and keep activity levels low
				Everyone else should avoid all physical activity outdoors

EPA-456/F-09-002

Air quality index: a guide to air quality and your health. EPA, August 2009

AQI air quality index

[a]People with heart or lung disease, children, or older adults

be contradictory, and this phenomenon remains incompletely understood. The true biological mechanisms leading to PM-induced pathology continue to be investigated. Also, while regional exposure data has become standard for PM epidemiology, studies with true individual exposure have yet to be fully realized. Finally, studies defining susceptible populations will help to shape further population-based recommendations.

Clinical Recommendations

When a patient presents with an acute illness, the clinician will not be able to determine the degree to which PM contributed. In illnesses where PM is known to contribute to risk, that percentage risk increase is usually measured in the single digits. Therefore, it is unlikely that there will ever be specific therapies for PM-related illness. Rather, health care providers should be familiar with prevention strategies for PM-related illness. Indoor PM exposure can be minimized by using air conditioning, particulate air filters, avoiding use of indoor combustion for cooking and heating, and smoking cessation [95]. Susceptible groups may benefit from limiting their outdoor exercise during peak traffic periods or poor air quality days [96]. The Air Quality Index (AQI) (http://airnow.gov) provides up-to-date information regarding local concentrations of PM and other pollutants. While government agencies have put out recommendations for minimizing PM exposure, peer-reviewed controlled data are limited for the implementation of these recommendations (Table 5).

Though PM exposure is ubiquitous, there is no defined and studied "safe" level. Patient education and behavioral modification strategies may contribute to better overall health. Additionally, these data can enable policy makers, after weighing the economic impact, to enforce or strengthen existing legislation that limits PM exposure. Volcanoes, forest fires, and other natural PM sources are part of our world and are unavoidable. However, by reducing modifiable PM exposure, we will likely see reductions in morbidity and mortality.

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Media centre

Household air pollution and health

Fact sheet N°292
Updated February 2016

Key facts

- Around 3 billion people cook and heat their homes using open fires and simple stoves burning biomass (wood, animal dung and crop waste) and coal.
- Over 4 million people die prematurely from illness attributable to the household air pollution from cooking with solid fuels.
- More than 50% of premature deaths due to pneumonia among children under 5 are caused by the particulate matter (soot) inhaled from household air pollution.
- 3.8 million premature deaths annually from noncommunicable diseases including stroke, ischaemic heart disease, chronic obstructive pulmonary disease (COPD) and lung cancer are attributed to exposure to household air pollution.

Indoor air pollution and household energy: the forgotten 3 billion

Around 3 billion people still cook and heat their homes using solid fuels (i.e. wood, crop wastes, charcoal, coal and dung) in open fires and leaky stoves. Most are poor, and live in low- and middle-income countries.

Such inefficient cooking fuels and technologies produce high levels of household air pollution with a range of health-damaging pollutants, including small soot particles that penetrate deep into the lungs. In poorly ventilated dwellings, indoor smoke can be 100 times higher than acceptable levels for fine particles. Exposure is particularly high among women and young children, who spend the most time near the domestic hearth.

Impacts on health

4.3 million people a year die prematurely from illness attributable to the household air pollution caused by the inefficient use of solid fuels (2012 data) for cooking. Among these deaths:

- 12% are due to pneumonia
- 34% from stroke
- 26% from ischaemic heart disease
- 22% from chronic obstructive pulmonary disease (COPD), and
- 6% from lung cancer.

Pneumonia
Exposure to household air pollution almost doubles the risk for childhood pneumonia. Over half of deaths among children less than 5 years old from acute lower respiratory infections (ALRI) are due to particulate matter inhaled from indoor air pollution from household solid fuels (WHO, 2014).

Stroke
Nearly one quarter of all premature deaths due to stroke (i.e. about 1.4 million deaths of which half are in women) can be attributed to the chronic exposure to household air pollution caused by cooking with solid fuels.

Ischaemic heart disease
Approximately 15% of all deaths due to ischaemic heart disease, accounting for over a million premature deaths annually, can be attributed to exposure to household air pollution.

Chronic obstructive pulmonary disease

Over one-third of premature deaths from chronic obstructive pulmonary disease (COPD) in adults in low- and middle-income countries are due to exposure to household air pollution. Women exposed to high levels of indoor smoke are more than 2 times as likely to suffer from COPD than women who use cleaner fuels. Among men (who already have a heightened risk of COPD due to their higher rates of smoking), exposure to indoor smoke nearly doubles (i.e. 1.9) that risk.

Lung cancer

Approximately 17% of annual premature lung cancer deaths in adults are attributable to exposure to carcinogens from household air pollution caused by cooking with solid fuels like wood, charcoal or coal. The risk for women is higher, due to their role in food preparation.

Other health impacts and risks

More generally, small particulate matter and other pollutants in indoor smoke inflame the airways and lungs, impairing immune response and reducing the oxygen-carrying capacity of the blood.

There is also evidence of links between household air pollution and low birth weight, tuberculosis, cataract, nasopharyngeal and laryngeal cancers.

Mortality from ischaemic heart disease and stroke are also affected by risk factors such as high blood pressure, unhealthy diet, lack of physical activity and smoking. Some other risks for childhood pneumonia include suboptimal breastfeeding, underweight and second-hand smoke. For lung cancer and chronic obstructive pulmonary disease, active smoking and second-hand tobacco smoke are also main risk factors.

Impacts on health equity, development and climate change

Without a substantial change in policy, the total number of people relying on solid fuels will remain largely unchanged by 2030 (World Bank, 2010). The use of polluting fuels also poses a major burden on sustainable development.

- Fuel gathering consumes considerable time for women and children, limiting other productive activities (e.g. income generation) and taking children away from school. In less secure environments, women and children are at risk of injury and violence during fuel gathering.
- Black carbon (sooty particles) and methane emitted by inefficient stove combustion are powerful climate change pollutants.
- The lack of access to electricity for at least 1.2 billion people (many of whom then use kerosene lamps for lighting) exposes households to very high levels of fine particulate matter, as well introduces other health risks, e.g. burns, injuries and poisonings from fuel ingestion, constraining other opportunities for health and development, e.g. studying or engaging in small crafts and trades, which require adequate lighting.

WHO's response

WHO provides technical support to countries in their own evaluations and scale-up of health-promoting household fuels and technologies. WHO is building capacity at the country and regional level to address household air pollution with workshops and the development of tools to help design, implement and monitor policies addressing household energy.

Other WHO activities include the following:

New indoor air quality guidelines for household fuel combustion

To ensure healthy air in and around the home, WHO's new indoor air quality guidelines for household fuel combustion provide health-based recommendations on the types of fuels and technologies to protect health as well as strategies for the effective dissemination of such home energy technologies. These build upon existing WHO outdoor air quality guidelines and WHO guidance on levels of specific indoor pollutants.

Household energy database

The WHO Household Energy Database is used to monitor global progress in the transition to cleaner fuels and stove combinations, as well as contributes to assessments of disease burden from household

energy and the energy access situation in low and middle-income countries. Recently this database has been expanded to include, in addition to extensive data on cooking, information on household fuels and technologies used for heating lighting and other impacts like time spent collecting fuel. The WHO Household Energy Database is used to monitor global progress in the transition to cleaner fuels and improved stoves as well as contribute to assessments of disease burden from household energy and the energy access situation in developing countries.

Research and programme evaluation

WHO is working with countries, researchers and other partners to harmonize methods of evaluation across settings so that health impacts are assessed consistently and rigorously and also incorporate economic assessment of health benefits.

Leadership and advocacy in the health, energy and climate community

Health sector
WHO is working to integrate guidance and resources for supporting clean household energy into global health initiatives and decision-support tools, such as the Global Action Plan for Pneumonia and Diarrheal Disease (GAPPD), or Global Strategy for Women and Children's Health, as well as into other aspects of WHO's own health policy guidance. WHO advocates about the compelling health arguments for cleaner household energy in a range of global forums addressing maternal and child health issues related to pneumonia as well as forums concerned with noncommunicable diseases in adults. This can help awareness of the importance of providing and scaling up of cleaner household energy as a core preventive public health measure.

Health and climate change
WHO is a partner of the Climate and Clean Air Coalition to Reduce Short-Lived Climate Pollutants (CCAC). As a member of the CCAC's health task force, WHO is providing technical support for harnessing health benefits from actions to reduce short-lived climate pollutants, and working to scale up health sector engagement to address such pollutants and improve air quality.

Health, energy and sustainable development
Reductions in air pollution-related disease burden (both for household and outdoor) will be used to monitor the progress towards attaining the Sustainable Development Goal on Health (SDG 3).

Ensuring universal access to clean fuel and technologies is a target of the Sustainable Development Goal on energy (SDG 7). If this target is met it could prevent millions of deaths and improve the health and well-being of the billions of people relying on polluting fuels and technologies for cooking, heating and lighting.

To better assess the health risks, as well as differentiated gender impacts from household energy, WHO is leading an effort with countries and surveying agencies (e.g. USAID's DHS, UNICEF'S MICS, World Bank's LSMS) to enhance, harmonize and pilot new questions for national censuses. The effort will also survey to better capture information on all the fuels and technologies used in the home for cooking, heating and lighting, as well as other impacts like time lost to fuel collection.

WHO also contributes to the development and updating of the global tracking framework used to measure progress toward the UN Secretary-General's Sustainable Energy for All initiative target of universal access to clean energy by 2030.

Sustainable Energy for All initiative

WHO also supports international initiatives to improve air pollution and related health impacts such as the Global Alliance for Clean Cookstoves and the Climate Clean Air Coalition.

For more information contact:

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Related links

WHO Household energy database

WHO's work on indoor air pollution

WHO's work on outdoor air
pollution

Lives-Saved tool (LiST)

Health in the green economy

Global Alliance for Clean
Cookstoves

Sustainable Energy for All
Initiative

Household air pollution

More about air pollution

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Effects of Air Pollution on Respiratory Diseases in India

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Abstract
Air pollution is the undesirable change in quality of air. In a developing country like India where majority of population lives in rural area, but both rural and urban areas are equally affected by pollution. Air pollution is largest environmental health risk that approximately kills 1 in 8 people globally, due to heart disease, stroke, respiratory disease and cancer. According to WHO air quality model (2016) about 92 % of world's population lives in places where air quality level exceed WHO limits. Particulate matter present in polluted air such as dust, smoke, pollen and volatile organic compounds trigger can cause serious damage to respiratory tract. When we breathe in dirty air, we bring air pollutants deep into our lungs; can trigger new cases of asthma. It can not only worsen a pre-existing respiratory illness, but also provoke the development of other diseases such as chronic illness, including chronic obstructive pulmonary disease, asthma and respiratory allergies, pulmonary hypertension, lung cancer etc., which can be fatal. By eating balanced and nutritious diet, not exposing to polluted area and wearing masks at a place where AQI is above the limit. Creating awareness about harmful effects of air pollution among people may be helpful to downscale its fatal effects.
Keywords- *Pollution, indoor, outdoor, AQI, biomass, particulate matter.*

Introduction

Air pollution is responsible for many health problems majorly in urban but also in some rural cities in India. According to WHO (World Health Organization) pollution is contamination of environment by any chemical, physical or biological agents that modifies the natural characteristics of atmosphere. Air pollution can be categorized into two categories, indoor and outdoor pollution which are presence of pollutants in air inside and outside the house respectively. Indoor cooking and heating with biomass fuels (agricultural residues, dung, straw and wood) or coal produces high levels of smoke that contains a various health-damaging pollutants. According to WHO Indoor air pollution is responsible for 2 million deaths annually. Outdoor air pollution is the result of inefficient combustion of fuels for transport, power generation and other activities. The World Health Organization (WHO) estimated 84000 deaths directly attributable to outdoor air pollution in Indian cities. Urban outdoor air pollution is estimated to cause 1.3 million deaths worldwide per year (WHO report on air pollution). Global urbanization which requires

large energy consumption has resulted in increased emissions into the atmosphere and a decrease in urban air quality [1]. Pollutants can be classified as primary or secondary. Primary pollutants are released directly into the atmosphere, whereas secondary pollutants result from chemical reactions among primary pollutants [2]. The air pollutants of most concern include nitrogen dioxide (NO_2), ozone and particulate matter (PM) [1]. PM is a general term that refers to a complex mixture of solids or liquids that vary in number, size, shape, surface area, chemical composition, solubility depending upon its place of production and mode of emission [3]. Particulate matter include inorganic compounds such as sulphates, nitrates, organic compounds such as polycyclic aromatic compounds and biological materials, such as pollen, bacteria, spores, and animal remains. On the basis of total suspended particle size, PM is classified as follows: constituent particles of up to 30 µm in diameter; constituent particles of less than 10 µm in diameter (PM_{10} or inhalable fraction); constituent particles of less than 2.5 µm in diameter ($PM_{2.5}$ or fine PM); and constituent particles of less than 10 nm in diameter ($PM_{0.1}$ or ultrafine PM) [4,5]. Current studies revealed a potential association between urban air pollutants and adverse health effects, particularly those that affect the respiratory and cardio-vascular systems [6,7].

Mechanism: How Air Pollution Affect the Respiratory System

Several mechanisms have been suggested to explain the adverse effects of air pollutants. Most widely accepted explanation is that, once in contact with the respiratory epithelium, high concentrations of oxidants and pro-oxidants in environmental pollutants such as PM of various sizes and compositions and in gases such as O_3 and nitrogen oxides cause the formation of oxygen and nitrogen free radicals. These pollutants in turn induce oxidative stress in the airways. These free radicals are neutralized by antioxidants such as vitamin C. In other words, an increase in free radicals that are not neutralized by antioxidant defenses initiates an inflammatory response with release of inflammatory cells and mediators (cytokines, chemokines, and adhesion molecules) that reach the systemic circulation, leading to inflammation, which not only has a negative effect on the respiratory system but also causes systemic effects [4,5]. Air pollutants also negatively and significantly harm lung development, creating an additional risk factor for developing lung diseases later in life.

a. Latent Period
The effects of pollutants on health can be acute or chronic. Acute effects are manifest shortly after exposure (hours or days). Chronic effects are usually assessed in longitudinal studies over years or decades [8].

b. Effects of Air Pollution on Children
Children are highly susceptible group to air pollutants. Children are more susceptile than adults because children have higher basal metabolic rates and engage in more physical activity than do adults, as well as because children spend more time outdoors than do adults. Also the volume of air passing through the airways of a child at rest is twice that of an adult under similar conditions. Pollutant-induced irritation producing a weak response in adults can result in significant obstruction in children. In addition, the fact that their immune system is not fully developed increases the possibility of respiratory infections [4,5,8-10].

c. Effects of Air Pollution during Pregnancy
During pregnancy exposure to air pollutants can impair foetal development and cause intrauterine growth retardation, premature birth, low birth weight, congenital anomalies, and, in cases that are more severe, intrauterine or prenatal death [11]. Maternal inhalation of pollutants can cause accelerated cell proliferation, prematurity and change in metabolism of foetus [12,13]. Another study revealed that a 1-µg/m3 increase in PM10 concentration and a 1-ppm increase in CO concentration were associated with a 0.6g and a 12g reduction in birth weight, respectively [14,15].

Diseases of Respiratory System

Asthma

Asthma, a chronic disease of the lungs characterized by inflammation and narrowing of the airways, causes a sensation of tightness in the chest, shortness of breath, wheezing, and coughing. If untreated, asthma episodes can be near fatal or even fatal [16]. For the past 40 years, the prevalence of asthma has increased in all countries in parallel with that of allergy. Asthma is still increasing worldwide as communities adopt modern lifestyles and become urbanized [13,53,54]. According to the WHO data published in may 2014 Asthma Deaths in India reached 151, 877 or 1.71% of total deaths. The age adjusted Death Rate is 17.16 per 100,000 of population ranks India #14 in the world. In a study among children between 6-18 years of age revealed that there is a significant association between traffic-related pollution and the development of asthma exacerbations and respiratory infections in children born to atopic parents and in those suffering from recurrent wheezing or asthma. These findings suggest that environmental control may be crucial for respiratory health in children with underlying respiratory disease [17]. The recent data base on asthma and traffic is less robust in adults [18]. A recent advance in assessing the effects of air pollution on asthma is the use of biomarkers of airway inflammation and oxidative stress as outcome measures in epidemiological studies [19-21]. With a projected increase in the proportion of the world's population living in urban areas, there is likely to be a marked increase in the number of people with asthma worldwide over the next two decades. Asthma affects approximately 300 million people worldwide. The costs of asthma are high in severe or uncontrolled asthma [22].

Chronic Obstructive Pulmonary Disease (COPD)

COPD is a progressive disease that makes it hard to breathe. Its symptoms include coughing that produce large amount of mucus, wheezing, shortness of breath and chest tightness. Among various causes of COPD, cigarette smoking is the leading one [23,24]. Chronic exposure to particulate pollutants may cause impaired lung growth in children. In a study of elderly people (≥65 years), it was found that short-term increases in O3 and PM10 concentrations were related to increased hospital admissions for COPD and pneumonia, especially during the warm season [25]. And it may be possible that the magnitude of effect increases with the days of exposure. In a multi-centric study in India, prevalence of COPD (chronic obstructive pulmonary disease) was 4.1%, with a male to female ratio of 1.56:1 and a smoker to non-smoker ratio of 2.65:1 in urban and the rural populations at Bangalore, Chandigarh, Delhi and Kanpur [26,27]. Particulate matter from fossil fuel combustion is air pollutants which can cause inflammation in the lung and further impaired the reduced pulmonary function in COPD patients [28]. Infection is one of the major factors which worsen COPD. In India, a study collecting data without spirometry assessment suggested that 12 million people were affected by COPD [29].

Lung Cancer

Lung cancer causes more deaths worldwide than any other cancer, with 1·8 million new cases and 1·5 million deaths in 2012. It is the most diagnosed cancer in men and third most common in women after breast and colorectal cancers [30]. Partial combustion of solid fuel produces large amount of particulate matter and carcinogenic gases. Epidemiologic studies have revealed that general air pollution, mainly due to the by-products of the incomplete combustion of fossil fuels, is associated with small relative increases in lung cancer. According to the WHO data published in Geneva in may 2014 Lung Disease Deaths in India reached 1,061,863 or 11.97% of total deaths. The age adjusted Death Rate is 126.99 per 100,000 of population ranks India #1 in the world. Lung cancer is often and accurately related to smoking. Smoking itself is one of the sources of air pollution in a closed space such as a room, besides its pathogenic role in the pathogenesis of COPD [31]. In smokers with asthma, lung function can be improved by

smoking cessation [32]. Inhalation exposure to airborne particulate matter in fine ranges ($PM_{2.5}$) is related to pulmonary dysfunction. In another study it was observed that each 10 µg/m3 elevation in fine particulate air pollution was associated with approximately 4%, 6%, and 8% increased risk of cardiopulmonary and lung cancer mortality respectively [33].

Low Vitamin D Status

Air pollution may have an indirect negative impact on vitamin D status. Vitamin D is majorly synthesized in the skin through the action of sunlight since vitamin D is found naturally only in a few food items [34]. Therefore, vitamin D status in humans is mainly determined by exposure to ultraviolet B (UVB) radiation, which initiates the conversion of 7-dehydrocholesterol to vitamin D3 [35]. Air pollution decreases the amount of sunlight that reaches the earth surface. According to a study, to reach an optimal vitamin D status in urban residents, the index of sun exposure was double that for rural residents [36]. This suggests that, in an urban environment, the amount of UVB reaching the earth is significantly decreased due to air pollution, which is the major factor in high prevalence of vitamin D deficiency. Deficiency of Vitamin D can promote multiple diseases, particularly osteoporosis but also cardiovascular disease, diabetes and cancer [37,38].

Measures to Reduce Negative Impact of Air Pollution

a. Nutritional solutions

Air pollution has been found to be associated with many fatal diseases both in urban and rural areas. In urban areas pollution is mainly due to industries, factories and TRAP (Traffic Related Air Pollution). Whereas, in rural areas it is due to household air pollution (HAP), burning of biomass and solid fuels. Diets characterized by a low intake of fruit, vegetables, wholegrain and fish, and an increased intake of processed foods, resulting in a nutrient intake that is low in beneficial nutrients such as antioxidants (e.g., carotenoids, vitamin D, E, falvinoids) and omega-3 PUFA [38,39]. This reduces

immunity against harmful effects of air pollution. It has been hypothesized that the intake of anti-oxidant and anti-inflammatory nutrients may improve various respiratory effects of air pollution through reductions in oxidative stress and inflammation [40]. Pollutants in air increase the production of reactive oxygen species (ROS) which in turn react with organic molecules and destroy them. Omega-3 PUFA intake from fish oil increases the activity of endogenous antioxidants which destroy excess of free radicals and reduce oxidative stress [41,42].

b. Preventive Measures

In a developing country like India, one of the major sources of rural pollution is household air pollution from cooking and heating practices. Clean LPG and electricity can be used as alternative to reduce pollution. People can reduce the time spent on outdoor activity when level of Air Quality Index [AQI] is beyond specified level [43]. Wearing personal protective equipment might be a useful for avoiding detrimental effect of ambient air pollutants [44]. Masks have been proved to be useful in reducing respiratory virus transmission [45]. Using of nose mask during haze environment can help people to prevent adverse effects from vehicular pollution [46].

Conclusion

India is a developing country which is progressing towards being developed. With the great progression one negative thing that is increasing along with is air pollution. Air pollution can create various diseases like asthma, COPD, lung cancer etc. one should try to reduce or compensate this by a positive thing like growing trees, by being less exposed to highly polluted places. A prudent diet is a key determinant to health throughout the whole life and could reduce the deleterious impact of air pollution on health. WHO launched The Global Alliance against Chronic Respiratory Diseases (GARD) is a voluntary alliance of national and international organizations, institutions and agencies committed to the vision of "a world where all people breathe freely". Incorporating the 'universal

access to clean fuel' agenda within the broader framework of rural development and raising the standard of living will go a long way in reducing disease burden.

.

Abbreviations

COPD: Chronic Obstructive Pulmonary Disease

TRAP: Traffic Related Air Pollution

PM: Particulate Matter

AQI: Air Quality Index

ROS: Reactive Oxygen Species

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INDOOR AIR POLLUTION IN INDIA – A MAJOR ENVIRONMENTAL AND PUBLIC HEALTH CONCERN

In many people's minds air pollution is associated with the contamination of urban air from automobile exhausts and industrial effluents. However, in developing countries, the problem of indoor air pollution far outweighs the ambient air pollution. There are four principal sources of pollutants of indoor air[1] : (i) combustion, (ii) building material, (iii) the ground under the building, and (iv) bioaerosols. In developed countries the most important indoor air pollutants are radon, asbestos, volatile organic compounds, pesticides, heavy metals, animal dander, mites, moulds and environmental tobacco smoke. However, in developing countries the most important indoor air pollutants are the combustion products of unprocessed solid biomass fuels used by the poor urban and rural folk for cooking and heating.

Approximately half the world's population and up to 90% of rural households in developing countries still rely on unprocessed biomass fuels such as wood, dung and crop residues[2]. A recent report of the World Health Organization (WHO) asserts the rule of 1000 which states that a pollutant released indoors is one thousand times more likely to reach people's lung than a pollutant released outdoors[3]. It has been estimated that about half a million women and children die each year from indoor air pollution in India[4]. Compared to other countries, India has among the largest burden of disease due to the use of dirty household fuels and 28% of all deaths due to indoor air pollution in developing countries occur in India[4].

The type of fuels used by a household is determined maily by its economic status. In the energy ladder, biomass fuels namely animal dung, crop residues and wood, which are the dirtiest fuels, lie at the bottom and are used mostly by very poor people. Electricity, which is the most expensive, lies at the top of ladder and it is also the cleanest fuel. The 1991 National Census for the first time inquired about the fuel used for coking. It revealed that about 90% of the rural population relied upon the biomass fuels like animal dung, crop residues and wood. A small portion used coal. Nation-wide about 78% of the population relied upon the biomass fuels and 3% on coal[5].

MAJOR AIR POLLUTANTS RELEASED FROM BIOMASS COMBUSTION

It has been estimated that more than half world's households cook their food on the unprocessed solid fuels that typically release at least 50 times more noxious pollutants than gas[6]. The stoves or *chullah* used for cooking are not energy efficient. The fuels re not burned completely. The incomplete combustion of biomass releases complex mixture of organic compounds, which include suspended particulate matter, carbon monoxide, poly organic material (POM), poly aromatic hydrocarbons (PAH), formaldehyde,

etc. The biomass may also contain intrinsic contaminants such as sulphur, trace metals, *etc*.

Particulates

In recent years a large number of studies of health impact of suspended particulate air pollution have been undertaken in developing countries[7.] These studies show remarkable consistency in the relationship observed between changes in daily ambient suspended particulate levels and changes in mortality. Smith[8] estimated the health risk from exposure to particulate air pollution by applying the mean risk per unit ambient concentrations based on the results of some urban epidemiological studies[9,10]. The range of risk was found to be 1.2 - 4.4% increased mortality per 10 mg/m^3 incremental increase in concentration of respirable suspended particles (PM_{10}). For the calculations of estimates, it was assumed that the health risk has linear relationship to exposure, the risk factors determined for urban centers of developed nations were used as standards; where the PM_{10} data were not available, 50% of suspended particulate matter (SPM) levels were considered as equivalent. The above assumptions may add to inaccuracy already inherent in such estimates.

Carbon Monoxide

Incomplete combustion of fuels produces carbon monoxide (CO). The CO and particle emission pose a serious problem when biomass fuels are used. Smith[11] has estimated that about 38, 17, 5 and 2 g/meal carbon monoxide is released during the household cooking, using dung, crop residues, wood and kerosene respectively. During the use of liquid petroleum gas (LPG) a negligible amount of CO is released. A study[12] by the National Institute of Occupational Health (NIOH), Ahmedabad reported indoor air CO levels of 144, 156, 94, 108 and 14 mg/m^3 air during cooking by dung, wood, coal, kerosene and LPG respectively. The short-term health effects of CO exposure are dizziness, headache, nausea, feeling of weakness, *etc*. The association between long-term exposure to carbon monoxide from cigarette smoke and heart disease and foetal development has been described by several authors[13,14].

Poly Organic Material and Poly Aromatic Hydrocarbons

Poly organic material is a loose term used to depict a group of chemicals having two or more rings. Of several chemicals included in this group, the PAHs have attracted interest for their possible carcinogenic effects. In addition

to PAH, azo and arino compounds have also been found to be potentially carcinogenic[15]. Most other categories of POM are of less environmental interest or are not found in large amounts in organic combustion products.

Polycyclic aromatic hydrocarbons constitute a large class of compounds released during the incomplete combustion or pyrolysis of organic matter[16]. They are often called polynuclear aromatic (PNA) because they contain three or more aromatic rings that share carbon atoms. Benzo(a)pyrene (BaP) is one of the most important carcinogen of the group. Often it is measured to indicate the presence or absence of PAHs although the relationship between BaP content and actual carcinogenicity may be weak[17]. Anthracene and phenanthracene are not carcinogens but methyl additions may render them carcinogenic. PAHs are activated by the hepatic microsomal enzyme system to carcinogenic forms that bind covalently to DNA[18].

Study by NIOH[19] showed that the indoor levels of PAH (total) during use of dung, wood, coal, kerosene and LPG were 3.56, 2.01, 0.55, 0.23 and 0.13 µg/m³ of air respectively. These PAH were fluorene, pyrene, chrysene, benzo(a)anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(a)pyrene, dibenz(ah) anthracene, benzo(ghi)perylene and indeno(1,2,3-cd) pyrene. All these PAHs except the first three have been classified as possible carcinogens.

Formaldehyde

Patel and Raiyani[12] measured levels of formaldehyde in indoor environment during cooking by different fuels. The formaldehyde mean levels were 670, 652, 109, 112 and 68 µg/m³ of air for cattle dung, wood, coal, kerosene and LPG respectively. The formaldehyde is well recognized to be an acute irritant and long-term exposure can cause a reduction in vital capacity and chronic bronchitis. The formaldehyde is well known to form cross-links with biologic macro-molecules. Inhaled formaldehyde forms DNA and DNA-protein cross-links in the nasal respiratory mucosa[20]. The formaldehyde has been shown to be carcinogenic in a dose dependent fashion in rodents[21,22]. The studies done in workers occupationally exposed to formaldehyde have consistently (11 of 13 studies reviewed) shown higher incidence of leukaemia[23]. In an epidemiological study in U.K., significantly excess mortality from lung cancer was observed in workers exposed to high levels of formaldehyde[24].

Mutagenic Activity of the Smoke Particulate Extract

Microbial tests are widely used as a screening tool for assessing mutagenic potential of chemical substances. The particulate matter in the smoke generated as a result of incomplete combustion of biomass fuels contains a number of organic compounds. To evaluate their carcinogenic potential, it is necessary to screen their mutagenicity through simple and rapid microbial assay as a first step.

Ames assay is simple and sensitive enough to measure mutagenicity of air-borne particulates, so that many researchers have applied this assay to demonstrate the ambient carcinogenic and mutagenic compounds in the extractable organic matter from air-borne particulates. Mutagenic response of complex mixtures of polycyclic organic matter from the combustion of biomass energy fuels was studied using tester strains TA 98 and TA 100 of *Salmonella typhimurium* which can detect the presence of frame-shift and base-pair mutagens[25]. The results indicated that the organic residues of smoke particulates of wood and cattle dung fuels contained direct acting frame-shift mutagens and cattle dung contained only direct acting base-pair mutagens while indirect acting frame-shift and base-pair mutagens were found to present in smoke particulates of both the energy fuels[26].

SPECIFIC DISEASES ASSOCIATED WITH INDOOR AIR POLLUTANT EXPOSURE

Respiratory illness, cancer, tuberculosis, perinatal outcomes including low birth weight, and eye diseases are the morbidities associated with indoor air pollution[27].

Respiratory Illness

The effect of air pollutants in general would depend on the composition of the air that is inhaled which will depend on the type of fuel used and the conditions of combustion, ventilation and duration for which the inhalation occur. The most commonly reported and obvious health effect of indoor air pollutants is the increase in the incidence of respiratory morbidity. Studies by the NIOH[28] on the prevalence of respiratory symptoms in women using traditional fuels (biomass) (n=175) and LPG (n=99), matched for economic status and age, indicated that the relative risk (with 95% C.I.) for cough, and shortness of breath (dyspnoea) was 3.2 (1.6-6.7), and 4.6 (1.2-18.2) respectively.

Childhood acute respiratory infections

Acute lower respiratory infections

Acute respiratory infections (ARIs) are the single most important cause of mortality in children aged less than 5 years, accounting for around 3-5 million deaths annually in this age group[30]. Many studies in developing countries have reported on the association between exposure to indoor air pollution and acute lower respiratory infections[31,32]. The studies on indoor air pollution from household biomass fuel are reasonably consistent and, as a group, show a significant increase in risk for exposed young children compared with those living in households using cleaner fuels or being otherwise less exposed[33]. Some of the studies carried out in India have reported no association between use of biomass fuels and ARI in children. In a case-control study in children under five years of age in south Kerala[34], where children with severe pneumonia as ascertained by WHO criteria were compared with those having non-severe ARI attending out patient department, the fuel used for cooking was not a significant risk factor for severe ARI. Non-severe ARI controls may represent the continuum (predecessor) of the cases themselves. Sharma *et al*[35] in a cross-sectional study in 642 infants dwelling in urban slums of Delhi and using wood and kerosene respectively, did not find a significant difference in the prevalence of acute lower respiratory tract infections and the fuel type.

Upper respiratory tract infections and otitis media

Studies on the relationship between indoor air pollution and acute upper respiratory infections in children both from developed[36,37] and developing nations[38,39] have not been able to demonstrate the relationship between the two. However, there is strong evidence that exposure to environmental tobacco smoke causes middle ear disease. A recent meta-analysis reported an odds ratio of 1.48 (1.08-2.04) for recurrent otitis media if either parent smoked, and one of 1.38 (1.23-1.55) for middle ear effusion in the same circumstances[40]. A clinic based case-control study of children in rural New York state reported an adjusted odds ratio for otitis media, involving two or more separate episodes, of 1.73 (1.03-2.89) for exposure to wood-burning stoves[41].

Chronic pulmonary diseases

Chronic obstructive pulmonary disease and chronic cor pulmonale

In developed countries, smoking is responsible for over 80% of cases of chronic bronchitis and for most cases of emphysema and chronic obstructive pulmonary disease. Padmavati and colleagues[42,43] pointed out to the relationship between exposure to indoor air pollutants and chronic obstructive lung disease leading to chronic cor pulmonale. These studies showed that in India, the incidence of chronic cor pulmonale is similar in men and women despite the fact that 75% of the men and only 10% women are smokers. Further analysis of the cases of chronic cor pulmonale in men and women showed that chronic cor pulmonale was more common in younger women. Chronic cor pulmonale seemed to occur 10-15 years earlier in women. The prevalence of chronic cor pulmonale was lower in the southern states than the northern states of India. This is attributed to higher ambient temperatures during most part of the year allowing for greater ventilation in the houses during cooking. The authors attributed this higher prevalence of chronic cor pulmonale in women to domestic air pollution as a result of the burning of solid biomass fuels leading to chronic bronchitis and emphysema which result in chronic cor pulmonale. Subsequent studies in India confirmed these findings[44,45]. Numerous studies from other countries, including ones with cross-sectional and case-control designs, have reported on the association between exposure to biomass smoke and chronic bronchitis or chronic obstructive pulmonary disease[46-52].

Pneumoconiosis

Pneumoconiosis is a disease of industrial workers occupationally exposed to fine mineral dust particles over a long time. The disease is most frequently seen in miners. Cases of respiratory morbidity who did not respond to routine treatment and whose radiological picture resembled pneumoconiosis have been reported in Ladakh[52,53]. However, there are no industries or mines in any part of Ladakh and therefore exposure to dust from these sources was ruled out[54,55]. Two factors considered responsible for the development of this respiratory morbidity were (i) Exposure to dust from dust storms. In the spring dust storms occur in many parts of Ladakh. During these storms the affected villages are covered by a thick blanket of fine dust, and the inhabitants are exposed to a considerable amount of dust for several days. The frequency, duration and severity of these dust storms vary considerably from village to village; (ii) Exposure to soot – due to the severe cold in Ladakh, ventilation in the houses is kept at a minimum. The fire place is used for both cooking and heating purposes. To conserve fuel during non-cooking periods, the wood is not allowed to burn quickly but is kept smouldering to prolong its slow heating effect. The inmates are thus exposed to high concentrations of soot.

The clinico-radiological investigations of 449 randomly selected villagers from three villages having mild, moderate and severe dust storms showed prevalence of pneumoconiosis of 2.0, 20.1 and 45.3% respectively. The chest radiographs of the villagers showed radiological characteristics which were indistinguishable from those found in miners and industrial workers suffering from pneumoconiosis. The dust concentrations in the kitchens without chimneys varied from 3.22 to 11.30 mg/m^3 with a mean of 7.50 mg/m^3. The free silica content of these dust samples was below 1%. Dust samples sufficient to allow measurement of the dust concentrations could not be collected during the periods of dust storms. A preliminary analysis of the settled dust samples collected immediately after the storms indicated that about 80% of the dust was respirable and the free silica content ranged between 60 and 70%. Detailed statistical analysis of the data showed that the frequency of dust storms, use of chimney in the houses and age were the most important factors related to the development of pneumoconiosis[56]. Thus, the results of medical and radiological investigations positively established the occurrence of pneumoconiosis in epidemic proportion. Exposure to free silica from dust storms and soot from domestic fuel were suggested as the causes of pneumoconiosis. Low oxygen levels or some other factor associated with high altitude may be an important contributory factor in causation of pneumoconiosis because it has been reported that the miners working at high altitude are more prone to develop pneumoconiosis than their counterparts exposed to the same levels of dust and working in the mines at normal altitude[57,58].

Lung Cancer

The link between lung cancer in Chinese women and cooking on an open coal stove has been well established[59-61]. Smoking is a major risk factor for lung cancer, however, about two-thirds of the lung cancers were reported in non-smoking women in China[62], India[63] and Mexico[64]. The

presence of previous lung disease, for example tuberculosis which is common in Indian women, is a risk factor for development of lung cancer in non-smokers[65]. The smoke from biomass fuels contain a large number of compounds such as poly aromatic hydrocarbons, formaldehyde, *etc.* known for their mutagenic and carcinogenic activities, but there is a general lack of epidemiological evidence connecting lung cancer with biomass fuel exposure. The factors associated with rural environment may have a modulating effect on the occurrence of lung cancer and therefore the low incidence of lung cancer in Indian women should not lead to a final conclusion of no link between biomass exposure and lung cancer. It may be concluded that at present there is limited evidence of indoor exposure from coal fires leading to lung cancer and there is no evidence for the biomass fuels. Further investigations are needed to reach definite conclusions.

Pulmonary Tuberculosis

Mishra *et al*[66] recently reported the association between use of biomass fuels and pulmonary tuberculosis on the basis of analysis of data collected on 260,000 Indian adults interviewed during the 1992-93 National Family Health Survey. Persons living in households burning biomass fuels were reported to have odd ratio of 2.58 (1.98-3.37) compared to the persons using cleaner fuel, with an adjustment for confounding factors such as separate kitchen, indoor overcrowding, age, gender, urban or rural residence and caste. The analysis further indicated that, among persons aged 20 years and above, 51% of the prevalence of active tuberculosis was attributed to smoke from cooking fuel. However, this study has inherent weakness that the cases of tuberculosis were self reported. There is strong possibility of false reporting as no investigation was done to confirm the reliability of the reporting. Gupta and Mathur[67] have reported similar findings from northern India. This study did not control for the confounding factors except for age.

There is experimental evidence to show that the exposure to wood smoke may increases susceptibility of the lungs to infections. Exposure to smoke interferes with the mucociliary defences of the lungs[68] and decreases several antibacterial properties of lung macrophages, such as adherence to glass, phagocytic rate and the number of bacteria phagocytosed[69,70]. Chronic exposure to tobacco smoke also decreases cellular immunity, antibody production and local bronchial immunity, and there is increased susceptibility to infection and cancer[71]. Indeed, tobacco smoke has been associated with tuberculosis[72,73].

Although the evidence in favour of tuberculosis associated with biomass fuel exposure is extremely weak, there is a theoretical possibility of such an association and considering the public health importance of the problem further experimental and epidemiological studies are necessary.

Cataract

During cooking particularly with biomass fuels, air has to be blown into the fire from time to time especially when the fuel is moist and the fire is smouldering. This causes considerable exposure of the eyes to the emanating smoke. In a hospital-based case-control study in Delhi the use of liquefied petroleum gas was associated with an adjusted odds ratio of 0.62 (0.4-0.98) for cortical, nuclear and mixed, but not posterior sub capsular cataracts in comparison with the use of cow dung and wood[74]. An analysis of over 170,000 people in India[75] yielded an adjusted odds ratio for reported partial or complete blindness of 1.32 (1.16-1.50) in respect of persons mainly using biomass fuel compared with other fuels after adjusting for socio-economic, housing and geographical variables; there was a lack of information on smoking, nutritional state, and other factors that might have influenced the prevalence of cataract. It is believed that the toxins from biomass fuel smoke are absorbed systematically and accumulate in the lens resulting in its opacity[27]. The growing evidence that environmental tobacco smoke causes cataracts is supportive[76,77].

Adverse Pregnancy Outcome

Low birth weight (LBW) is an important public health problem in developing nations attributed mainly to under-nutrition in pregnant women. Low birth weight has serious consequences including increased possibility of death during infancy. Exposure to carbon monoxide from tobacco smoke during pregnancy has been associated with LBW. Levels of carbon monoxide in the houses using biomass fuels are high enough to result in carboxyhaemoglobin levels comparable to those in smokers[78,79]. In rural Guatemala, babies born to women using wood fuel were 63 g lighter than those born to women using gas and electricity, after adjustment for socio-economic and maternal factors[80]. A study carried out in Ahmedabad reported an excess risk of 50% of stillbirth among women using biomass fuels during pregnancy[81]. An association between exposure to ambient air pollution and adverse pregnancy outcome has been widely reported[82-84].

Considering the association of LBW with a number of disease conditions later in life, there is a need for further studies.

INTERVENTION

Adequate evidence exists to indicate that indoor air pollution in India is responsible for a high degree of morbidity and mortality warranting immediate steps for intervention. The intervention programme should include (i) Public awareness; (ii) Change in pattern of fuel use; (iii) Modification in stove design; (iv) Improvement in the ventilation; and (v) Multisectoral approach.

Public Awareness

The first and the most important step in the prevention of illnesses resulting from biomass fuels is to educate the public, administrators and politicians to ensure their commitment and promoting awareness of the long-term health effects on the part of users. This may lead to people finding ways of minimizing exposure through better kitchen management and infant protection.

Change in Pattern of Fuel Use

The choice of fuel is mainly a matter of availability, affordability and habit. The gobar gas plant which uses biomass mainly dung has been successfully demonstrated to produce economically viable quantities of cooking gas and manure. Recently, the Government of Andhra Pradesh has introduced a programme called the Deepam Scheme to subsidize the cylinder deposit fee for women from households with incomes below the poverty line to facilitate the switch from biomass to LPG. Such schemes will encourage the rural poor to use cleaner fuels. The use of solar energy for cooking is also recommended.

Modification in Stove Design

Use of cleaner fuels should be the long-term goal for the intervention. Till this goal is achieved, efforts should be made to modify the stoves to make them fuel efficient and provide them with a mechanism (*eg* chimney) to remove pollutants from the indoor environment. Several designs of such stoves have been produced. NIOH study showed significant decrease in levels of SPM, SO_2, NO_x and formaldehyde with specially designed smokeless stoves in comparison with traditional cooking stoves[12]. However, they have not been accepted widely. Large scale acceptance of improved stoves would require determined efforts. The most important barriers to new stove introduction are not technical but social[85].

Improvement in Ventilation

In many parts of the country poor rural folk are provided with subsidized houses under various government/international agencies aided schemes. Ventilation in the kitchen should be given due priority in the design of the houses. In existing houses, measures such as putting a window above the cooking stove and providing cross ventilation through the door may help in diluting the pollution load.

Multisectoral Approach

Effective tackling of indoor air pollution requires collaboration and commitment between agencies responsible for health, energy, environment, housing and rural development.

CONCLUSIONS

Indoor air pollution caused by burning traditional fuels such as dung, wood and crop residues causes considerable damage to the health of particularly women and children. There is evidence associating the use of biomass fuel with acute respiratory tract infections in children, chronic obstructive lung diseases, and pneumoconiosis in the residents of Ladakh villages. Lung cancer has been found to be associated with the use of coal in China, however, there is no evidence associating it with the use of biomass fuels. Cataract and adverse pregnancy outcome are the other conditions shown to be associated with the use of biomass fuels. The association of tuberculosis and chronic lung infections with the use of biomass fuels has not been proved.

Finally, there is enough evidence to accept that indoor air pollution in India is responsible for a high degree of morbidity and mortality warranting immediate steps for intervention. The first and the most important step in the prevention of illnesses resulting from the use of biomass fuels is to educate the public, administrators and politicians to ensure their commitment for the improvement of public health. There is utmost requirement to collect better and systematic information about actual exposure levels experienced by households in different districts and climatic zones and develop a model for predicting the exposure levels based on fuel use and other household data therein (exposure atlas) to protect the health of children, women and elderly persons.

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How Air Pollution Contributes to Lung Disease

When we breathe in dirty air, we bring air pollutants deep into our lungs, so it's no surprise that air pollution causes serious damage to the respiratory tract. Air pollution exposure can trigger new cases of asthma, exacerbate (worsen) a previously-existing respiratory illness, and provoke development or progression of chronic illnesses including lung cancer, chronic obstructive pulmonary disease, and emphysema. Air pollutants also negatively and significantly harm lung development, creating an additional risk factor for developing lung diseases later in life.

Asthma
Over 20 million people in the U.S., including six million children now gasp for breath due to asthma. Asthma, a chronic disease of the lungs characterized by inflammation and narrowing of the airways, causes a sensation of tightness in the chest, shortness of breath, wheezing, and coughing. If untreated, asthma episodes can be near-fatal or even fatal. Asthma is not currently curable, and damage that is done to lung tissue during asthma attacks may lead to permanent damage. Nearly 1.8 million emergency room visits were attributed to asthma in 2005. There are many triggers to asthma attacks, including dust, smoke, pollen, and volatile organic compounds. Common outdoor pollutant triggers include ozone, carbon monoxide, sulfur dioxide and nitrogen oxides.

The Asthma-Ozone Connection
Ozone, one of the most widespread air pollutants in the US, is formed when volatile organic compounds react with nitrogen oxides in the presence of sunlight. Ozone irritates the lungs at concentrations which are fairly common in urban settings, particularly in summer months. Increases in ozone are linked to asthma and other lung diseases. For those with severe asthma, symptoms increase even when ambient ozone levels fall under the thresholds set by the EPA. Elevated ozone levels also aggravate pre-existing heart problems, like angina.

Chronic Obstructive Pulmonary Disease (COPD), chronic bronchitis and emphysema
Chronic Obstructive Pulmonary Disease (COPD) is another condition characterized by narrowing of the airways, but these changes are permanent rather than reversible. COPD is caused by exposure to pollutants that produce inflammation, an immunological response. In larger airways, the inflammatory response is referred to as chronic bronchitis. In the tiny air cells at the end of the lung's smallest passageways, it leads to destruction of tissue, or emphysema. Although current and ex-smokers account for most patients with COPD, exposure to air pollutants plays an important role in the development of COPD and the origin and development of acute exacerbations.

Lung Cancer
Lung cancer, the leading U.S. cancer killer in both men and women, is often (and accurately) associated with smoking tobacco. While that's true, there are multiple other risk factors for developing lung cancer, including air pollution. Particulate matter and ozone in particular may affect mortality due to lung cancer.

Children are Especially Vulnerable
Children are particularly susceptible to the effects of air pollution. They breathe through their mouths, bypassing the filtering effects of the nasal passages and allowing pollutants to travel deeper into the lungs. They have a large lung surface area relative to their weight and inhale relatively more air, compared to adults. They also spend more time out of doors, particularly in the afternoons and during the summer months when ozone and other pollutant levels are at their highest. And, children may ignore early symptoms of air pollution effects, such as an asthma exacerbation, leading to attacks of increased severity. Combine those factors with the adverse impact of some pollutants on lung development and the immaturity of children's enzyme and immune systems that detoxify pollutants, and you have a series of factors that contribute to children's increased sensitivity to air pollutants.