Selected Papers of Beijing Forum 2005

Ambient Air Pollution and Adverse Health Effects

Herman Autrup

University of Aarhus, Denmark

INTRODUCTION

Pollution of the air have been known since the early man discovered fire and started to use biomass for heating and preparing food. However, many people consider that ambient air pollution is a modern phenomenon linked to industrial development, although health problems related to air pollution have been known before the industrial age. London has always been considered synonymous with air pollution due to heavy industrial activity and use of poor quality coal for heating and industrial purposes. The famous London smog (smoke and fog) in 1950, which was mainly due to particles and sulfur dioxide, resulted in a significantly increased mortality. Today, such pollution episodes are much less frequent in developed Western countries, whereas they still occur in some Asia countries with very high levels of air pollution due to the burning of biomass and very high daily concentrations, especially during the winter. The London smog episode became the catalyst for modern air pollution research and regulation of air pollution based upon health outcome. It is now widely accepted that exposure to outdoor air pollution is associated with a broad range of acute and chronic health effects, ranging from minor physiological disturbances to death from respiratory and cardiovascular diseases.

The World Health Organization (WHO) estimates that urban air pollution contributes to approximately 800,000 death and 4.6 million lost life-years (DALY) worldwide (WHO 2002). However, this burden is not distributed equally globally, and it is assumed that the problem in Asia is greater. However, a concern is that these estimates are mainly based upon US data and not Asian data. A large regional variation in the estimated disease burden has been reported, and air pollution is estimated to account for 5.9% of the total DALY’s in East Asia, and 3.7% in South East Asia, and urban outdoor air pollution is responsible for 1.4% and 0.55% respectively, with household air pollution being of the greater concern. The health effects of outdoor air pollution in developing countries of Asia have recently been reviewed by the Health Effect Institute (HEI, 2004). In spite of this greater risk associated with in-door air pollution the focus on this paper will be on ambient outdoor air pollution.

Exposure to air pollution

In general, combustion is the chief process responsible for pollutant emissions. The chemical composition of air pollution is very complex and consist of gases, e.g. nitrogen oxides, sulfur dioxide, ozone, carbon monoxide, carbon dioxide and particles. Combustion processes are mainly responsible for the pollutant present in ambient air. However, incomplete combustion and spill, e.g. gasoline, may also contribute to ambient air pollution, e.g. benzene. Focus has mostly been on combustion of fossil fuel in connection with energy production and transportation. However, combustion of garbage and biomass, e.g. forest fires will also contribute to the air pollution. Combustion of garbage is especially a problem in poorer areas and villages; as the combustion temperature and technology is not sufficient, many unwanted products are formed.

Some of the highest levels of air pollution in the world are found in Asian megacities, and the level appears to be closely linked to social and economic development, e.g. industrialization, population growth, urbanization.
levels also exceed the WHO guideline values (KEI, 2004). It is difficult to analyze the health effects associated with the individual component as complex interactions will occur.

**Particles**

Urbane airborne particulate matter is a variable mixture of numerous classes and subclasses of contaminants. Particle properties and their associated health effects differ by size. The size and associated composition of particles determine their behavior in the respiratory system, i.e., penetration, deposition and clearance. The particle size is one of the most important parameters in determining the residence and spatial distribution of particles in ambient air. Ultrafine particles have a very short life, but will rapidly accumulate to form larger particles, that can be transported thousands of kilometers and remains in the atmosphere from days to weeks. In contrast, coarse particles will settle rapidly from the atmosphere and are not readily transported long distances, except under special conditions, i.e., Asian dust.

Particles consist of a core to which numerous other compounds, organic as well as inorganic are associated, e.g., nitrogen oxide reacts to form nitrate and sulfur dioxides to form sulfates. These secondary particles do have diverging toxicity from the original particle (Schlesinger and Cassee, 2003).

The particulate matter (PM) fraction has been divided into two principal groups according to their aerodynamic diameter: coarse particles and fine particles, and fine particles are less than 2.5 um (PM2.5) and coarse particles represent particles in the range 2.5-10 um (PM2.5-10). Some studies suggest that fine particles are more biologically active than coarse PM, but the relative importance of fine and coarse PM may depend on specific sources present in some areas but not in others. Furthermore, it is assumed that the fine particles are a better measure for anthropogenic activity than the coarse. Recently, focus has been on the ultrafine particles (PM<0.1 (M) that have also been named nanoparticles. These particles are a serious health concern as they are deposited in the alveoli and can pass through the lining of the lung and be distributed systemically in the body. The toxicity of the nanoparticles is also anticipated to be more toxic due to its larger number and surface area per mass unit than the PM2.5. The most commonly reported indicator of particulate pollution is the concentration of total suspended particulates (TSP), and a WHO guideline value based upon TSP (90 ug/m3) has been established. This level is commonly exceeded in many of the Asian megacities.

Different sources contribute to the PM, vehicle exhaust and combustion of biomass being the most important sources. The emissions of motorcycle exhaust (ME) are a major source of air pollution in areas, where motorcycles are a popular mean of transportation. The 2-and 4-stroke motorcycle engines have smaller capacity and poorer combustion efficiency than diesel and gasoline engines. Two stroke engines are also widely used in a variety of applications, including outboard boat motors, lawn movers and motor saws.

The extract of ME particles induces various biological responses relevant for inflammatory processes (Ueng et al, 2005).

Numerous studies on organic extracts of urban particulate matters have proven not only mutagenicity, but also different adjuvant activity in conjunction with a reference allergen, with large regional and seasonal variations (Cassoni et al, 2004; Steerenberg et al, 2005). The reported regional and seasonal variations indicate the difficulties in the analysis of epidemiological studies on particulate matters, as a particle is not just a particle.

Long-term exposure to current ambient PM concentrations may lead to a marked reduction in life expectancy, and the reduction in life expectancy is primarily due to increased cardio-pulmonary and lung cancer mortality. Chronic exposure for PM2.5 has been associated with increased mortality even at low level, and is associated with decreased lung function, decreased cystolic blood pressure and increased heart rate at high level of PM (Ebelt et al, 2005).

Particulate matters from dust storms that originate in the Mongolian region of China have raised concern within China and in its neighboring countries. An increased mortality risk for respiratory and cardiovascular diseases has been reported in elderly Korean during the Asian dust event (Kwon et al, 2002). These particles have also been observed as far away as the North American west coast. Experimental studies in rats, i.e. IL-6 pulmonary hypertensive rats, have shown an increase in inflammatory markers. It was concluded that Asian dust storm particles might cause pulmonary inflammation and injury and possibly a systemic response (Lei et al, 2004)

**Polycyclic aromatic hydrocarbons**

Polycyclic aromatic hydrocarbons are principal pollutants formed by incomplete combustion and are associated with particulate matters. Numerous studies on the level of PAH have been conducted all over the world. This group contains several compounds of which many are carcinogenic in experimental animals. For comparative purposes,
carcinogenic benzo(a)pyrene is used as the reference compound, although it is not specific for traffic generated PAHs. Large regional and local variation in the level of specific PAH has been seen in Asia, Africa and the Western hemisphere (Norramit et al, 2005; Georgiadis et al 2001; Fanyo et al, 2005). Based upon the toxic equivalent principle for PAHs and WHO Unit risk factor for PAH, the exposure for PAH is associated with an increased risk of lung cancer among Bangkok residents (Ruchirawat et al, 2002).

**Diesel exhaust**

Polycyclic aromatic hydrocarbons are products of incomplete combustion and are commonly found in diesel exhaust. Pollutants in diesel exhausts exist as particles and gas phase compounds. The mutagenic activity is primarily due to direct acting compounds, such as mono-and dinitropyroaromatic compounds. This group of compounds accounts for up to 40% of the total bacterial mutagenicity present in ambient air. One of these compounds is 3-nitrobenzantrone, which appears to be specific for diesel exhaust (Arlt et al, 2001). The relative level of unsubstituted and substituted PAH and mutagenic activity depends on a number of factors, e.g. engine type, driving conditions and to a lesser extent of fuel type (Johansen, 1997).

Exposure to diesel exhaust has been associated with an increased risk of bladder cancer in workers occupationally exposed to high level of diesel exhaust, e.g. operators of heavy machinery and truck/bus drivers (Bofetta et al, 2001).

In experimental studies, inhalation of diesel engine exhaust has also been shown to reduce bacterial clearance and increase the risk of infection (Harrod et al, 2005).

**Sulfur dioxide**

Sulfur dioxide (SO2) is a gaseous by-product of the combustion of fossil fuels that contains sulfur, e.g. certain coals, liquid fuels and natural gas. Exposure to SO2, even at low level is linked to increased bronchoconstriction in people with asthma, and reduction in lung function has been observed at higher concentrations. Long-term exposure to SO2 has been associated with decreased pulmonary function and increased mortality (Krewski et al, 2000).

**Nitrogen dioxide**

Nitrogen dioxide (NO2) is a gaseous by-product of the combustion of fossil fuels. In many urban areas mobile source emissions are the major source of NO2. NO2 is more likely to reach the lower airways compared to SO2 due to its lower water solubility. Furthermore, NO2 may also react as an oxidant. Exposure even at low levels induces inflammatory responses and increased responsiveness to ozone and allergens have been reported. Short-term exposure is associated with increased mortality and hospital admissions (Ackermann-Liebrich and Rapp, 1999)

**Adverse health effects**

Outdoor air pollution contributes to various adverse health effects. Whereas some effects may be related to short-term exposure, others have to be related to long-term exposure. Although the biological mechanisms are not fully elucidated, epidemiological studies suggest a link between air pollution and various health outcomes, e.g. respiratory symptoms, mortality, cancer. The relative risks related to air pollution, however, are rather small.

**Mortality**

A large body of epidemiological evidence suggests an association between ambient air pollution and cardiovascular mortality and morbidity, but the majority of these studies have been conducted in the developed Western world. The major risks have been linked to SO2 and PM. Sulfur dioxide is associated with increased daily mortality from both respiratory and cardiovascular disease even at the low levels now observed in the Western hemisphere.

Large cohort studies, using the same protocol, have been conducted in Western Europe based upon 29 cities (APHEA; Katsouyanni et al, 2001) and the US based upon 90 cities (NMMAPS; Samet et al, 2000), while a small number of studies have been conducted in Asia. The estimates of percent change per 10 ug/m3 increase in pollutant concentration on all-cause mortality showed slight variation, ranging from 0.41 in Asia and US to 0.6 in Europe for PM10, whereas it was 0.35 for Asia and 0.40 in Europe for SO2. PM2.5 appears to be more closely associated with mortality than PM10 or total suspended particulate matters (TSP). However, most of these studies have been conducted in the US (Pope et al, 2002). There are some concern using these data for estimation of risk in other populations due to difference in methods collecting and analyzing the concentrations of the particle and the chemical composition, e.g. different sources, different ratio between fine and coarse particles.
Long term exposure to ambient PM contributes to systemic inflammatory pathways, which are relevant aspects of atherogenesis resulting in atherosclerosis and ultimately cardiovascular death. Carotid artery intima-media thickness (CIMT) is normally considered a risk indicator of atherosclerosis. A recent epidemiological study has shown an association between PM2.5 and CIMT, and indirectly the risk of atherosclerosis. The risk was higher in women with a 15% increase in CIMT for a 10 ug/m³ increase in PM2.5 (K nzli et al, 2005).

Increased risk for infant and child mortality from respiratory diseases has been associated with exposure to air pollution both in developed and developing countries (Romieu et al, 2002).

**Respiratory disorders**

Exposure to traffic related air pollution has been implicated in impairment of respiratory health in children. Truck traffic and air pollutants associated with truck traffic were associated with chronic respiratory symptoms in Dutch school children living close to motorways, whereas there was no association with car traffic. Furthermore, there was no association with bronchial hyperresponsiveness in these children, however sensitization to outdoor allergen was increased in the group exposed to high level of air pollution (Janssen et al, 2003). The increased sensitivity to outdoor allergen may be a consequence of the fact that diesel exhaust particles modifies the allergen and enhances the immunologic response of the allergen and increase the inflammatory responses as demonstrated both in animal studies and human volunteer studies (Diaz-Sanchez et al, 2000).

Air pollution has not been found to induce asthmatic conditions in children, but will exuberate an already existing condition.

**Cancer**

Epidemiological studies have indicated that in Western countries the relative risk of developing lung cancer is 1.5-fold higher in urban that in rural areas after adjusting for cigarette smoking. Air pollution, e.g. vehicles, industry, power plants, has been reported to increase the risk of lung cancer (Vinies et al, 2004). The risk of lung cancer death has been suggested to increase by 8% for every 10 micrograms of fine particles/m³ of inhaled air (Nafstad et al, 2003). Epidemiological studies have also shown strong support for that the higher risk of lung cancer among non-smoking women in Xuanwei County, China is associated with the use of smoky coal for cooking and heating in homes without chimneys. The smoke of smoky coals is high in carcinogenic PAH (Keohavong et al, 2005).

**Exposure assessment**

Numerous epidemiological studies have reported association between outdoor concentrations of air pollutants and adverse health effects. Most studies have been using ambient monitoring data to estimate exposure. However, in case of PM, personal exposure is dominated by indoor sources especially taking into consideration that people spent up to 90% of their time indoor, thus the validity of using ambient concentrations as an exposure estimate may introduce misclassification. The risk of misclassification is less for gaseous air pollutants except in cases where a significant in-door source is present, e.g. nitrogen oxides. An alternative to ambient and personal measurement is the use of biomarkers to assess exposure, and a further advantage of these biomarkers is that they also reflect the time-activity pattern.

**Biomarkers**

The ultimate biomarker represents both an accurate exposure estimate and is also an indicator of health. Several biomarkers have been developed to assess exposure for genotoxic compounds in ambient air. Some of these biomarkers represent the exposure for specific compounds, e.g. benzene in blood and urine, and its metabolites, muconic acid and phenylmercapturic acid, in urine. However, the level of these products is not linked to the genotoxic effect. 1-hydroxypyrene (1-HOP) is another commonly used biomarker for PAH exposure although pyrene is not specific for ambient air pollution and can also be found in food. The carcinogenic PAH found to be associated with particles are metabolized to reactive molecules that can react with DNA to form bulky-DNA adducts. DNA adducts tend to be higher among subjects heavily exposed to urban and occupational pollutants (Autron et al, 1999; Peluso et al, 2001). PAH-DNA adducts have also been detected in the blood from newborns, whose mothers were living in polluted areas of Poland and China. The adduct level was similar in mothers and in the child (Perera et al, 2005) suggesting that carcinogenic agents present in ambient can pass the placental barrier and initiate damage in the unborn child that is relevant for carcinogenesis. A positive association has been established between the level of PAH in ambient air and the bulky adduct level at medium to high level of PAH, but not at the low level situation generally observed at ambient pollution. A weak but positive association has been
established between the bulky adduct level and risk of development of lung cancer (Peluso et al, 2005; Bak et al, 2005) Particles generated by combustion are composed of a carbon core to which other compounds such as metals and PAH adhere. The particles do induce oxidative stress mediated by a particle-induced inflammation causing macrophages to release ROS. Oxidative stress to DNA is frequently measured as 8-oxodG. In a study among human volunteers we found a positive association between individual PM exposure and 8-oxodG, whereas no association was found between amount of PM and bulky adducts (S rensen et al, 2003). One of the consequences of DNA adducts, when un-repaired, is the induction of mutations that may ultimately induce cancer formation. An increased frequency of mutations in the p53 cancer suppressor genes has been observed both in the sputum of individuals exposed to smoky coal emission and in lung tumors from people in the region. The most frequently observed mutation seen in this group is a G to T transversion that is commonly associated with exposure to carcinogenic PAH (Keohavong et al, 2005).

Susceptible populations

Increased risk for adverse health effects due to air pollution could be related either to higher dose, acquired predisposing diseases and genetic susceptibility.

In the group exposed to higher dose are people living or working along highly trafficked roads, people with long commuting hours, or people who are occupationally exposed, e.g. bus drivers, traffic police officers. This group does also include children as their body burden with air pollutants is higher than adduct due to a relative high ventilation rate.

Elderly subjects, and especially subjects with pre-existing heart and lung disease are more susceptible to the effect of short-term ambient air pollution on mortality and morbidity. Asthmatics do also respond stronger than non-asthmatic on increase in air pollution, particularly PM. In case of long-term exposure, socially disadvantaged and poorly educated populations respond more strongly in term of mortality.

The toxic effects of air pollutants are modified by genetic variation in genes involved in, e.g. inflammatory processes, defense against reactive oxygen species formed by particulate matters, enzymes involved in the detoxification of PAH and other toxic compounds present in ambient air.

Prevention

Improving air quality will improve the quality of life and have important impact on economic development. Mobile sources are the major contributor to ambient air pollution in developed countries. Thus, stringent standards for new sources of air pollution (especially motor vehicles) will significantly improve air quality. However, the increasing economic welfare will result in an increasing number of vehicles and longer commuting distances, so the net benefits of these standards may be negligible. As the level of the pollution depends on the engine type and condition, fuel type, traffic congestions, driving habits and load of vehicles stricter control and introduction of cleaner technologies, e.g. hybrid cars. Furthermore, improved city planning to minimize traffic congestions and development of public transportation may help in minimize the air pollution in the megacities and improve the quality of life.

References
