Air Pollution and Health in Urban Areas

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SUMMARY

In this paper, recent reviews of the World Health Organization, other review papers, and more recent literature on the human health effects of current air pollution trends in urban areas are reviewed and summarized as follows:

Sulphur dioxide. **Some studies, but not others, found associations between sulphur dioxide (SO_2) exposure and daily mortality and morbidity. Single-pollutant correlations sometimes disappeared when other pollutants, especially suspended particulate matter (SPM), were included. Cross-sectional studies with asthmatics revealed significant, non-threshold relations between SO_2 and decrements of the forced expiratory volume in 1 second (FEV_1).**

Nitrogen dioxide. **Weak associations between short-term nitrogen dioxide (NO_2) exposure from gas cooking and respiratory symptoms and a decrement in lung function parameters were found in children, but not consistently in exposed women. With long-term exposure, children, but not adults, exhibit increased respiratory symptoms, decreased lung function, and increased incidences of chronic cough, bronchitis, and conjunctivitis. A causal relationship between NO_2 exposure and adverse health effects has not yet been established.**

Carbon monoxide. **Binding of CO in the lungs with hemoglobin in the blood forms carboxyhemoglobin (COHb), which impairs the transport of oxygen. The health effects of CO include hypoxia, neurological deficits and neurobehavioral changes, and increases in daily mortality and hospital admissions for cardiovascular diseases. The latter persists even at very low CO levels, indicating no threshold for the onset of these effects. Whether the relation between daily mortality and exposure to CO are causal or whether CO might act as a proxy for SPM is still an open question. Ambient CO may have even more serious health consequences than does COHb formation and at lower levels than that mediated through elevated COHb levels.**

Ozone. **Short-term acute effects of O_3 include pulmonary function decrements, increased airway responsiveness and airway inflammation, aggravation of pre-existing respiratory diseases like asthma, increases in daily hospital admissions and emergency department visits for respiratory causes, and excess mortality. Exposure-response relations are non-linear for the respective associations between O_3 and FEV_1, inflammatory changes, and changes in hospital admissions, whereas the relation between percent change in symptom exacerbation among adults and asthmatics is linear. Single-pollutant associations between O_3 exposure and daily mortality and hospital admissions for respiratory diseases is statistically significant, even in multi-pollutant models.**

Suspended particulate matter. **Associations between SPM concentrations and mortality and morbidity rates are significant. The acute health effects of SPM, even at short-term low levels of exposure, include increased daily**

mortality and hospital admission rates for exacerbation of respiratory disease, fluctuations in the prevalence of bronchodilator use, and cough and peak flow reductions, as well as long-term effects with respect to mortality and respiratory morbidity. Such effects depend on particle size and concentration and can fluctuate with daily fluctuations in PM_{10} or $PM_{2.5}$ levels. The relation between PM_{10} or $PM_{2.5}$ exposure and acute health effects is linear at concentrations below 100 $\mu g/m^3$. Currently no threshold has been reported below which no effects occur. The influence of co-polluting gaseous pollutants could explain part of the observed variance in short-term health effects and reduce the contribution of SPM.

Lead. **The biological effects of lead can be related to blood lead levels, the best indicator of internal exposure. The potential effects of lead in adults and children include encephalopathic signs and symptoms, central nervous system symptoms, cognitive effects, increased blood pressure, and reduced measures of child intelligence. Whereas the lowest-observed-effect-levels are established for most health effects, the question of increased blood pressure is still controversial. That low levels of lead exposure may result in mental deficit has also been a controversial subject of recent debate.**

KEYWORDS

sulphur dioxide, nitrogen dioxide, ozone, lead, carbon monoxide, suspended particulate matter, health effects

INTRODUCTION

In urban environments of developed and developing countries, ambient air pollution influences the life of the people. According to recent publications, based on a study of Hong in 1995 (personal communication), about 1.5 billion people are exposed to increased ambient air pollutant concentrations of suspended particulate matter (SPM), sulphur dioxide (SO_2), and ozone (O_3) /1–4/. In developed countries, the health impacts of ambient air pollution are well recognized. In populations of developing countries with an extensive use of coal for combustion and growth of the number of motor vehicles, awareness of the health impact of air pollution is still low. Ambient air pollution is only slowly being recognized as a problem of daily concern for everyone living in urban areas of developing countries. Nevertheless, because of the magnitude of the air pollutant concentrations observed in such areas, serious health effects are expected in the populations living there.

In developed countries, residents are exposed to indoor air pollution from combustion products, household chemicals, airborne bacteria and viruses, and radon and its daughters. In developing countries, ambient air pollution is significant in urban areas. In addition, indoor combustion of coal, firewood, and other biomass fuels for cooking and heating has resulted in high concentrations of SPM, SO_2, and carbon monoxide (CO) in urban and rural areas. These indoor air pollutant concentrations are often above ambient concentrations by at least an order of magnitude /5/.

In this paper, a synopsis is presented of the health effects that are caused by air pollution in urban areas. The air pollutant situation in these countries is characterized by using the data of the Air Management Information System (AMIS) data base that contains recent summary data on air pollutant concentrations in more than 100 cities in the world /6–8/. Under the umbrella of the Healthy Cities Programme, the AMIS was set up in 1996 by WHO as a successor of the UNEP/WHO/ Global Environmental Monitoring System/Air

(GEMS/AIR /9/). AMIS has the objective of transferring summary information on air quality management (air quality management instruments used in cities, indoor and ambient air pollutant concentrations, air-pollution-induced health effects, control actions, air quality standards, emission standards, emission inventories, dispersion modeling tools, and noise levels) among countries and cities /8/. AMIS data can be used for comparing the air pollutant situation in various urban areas of the World as a means to estimate the exposure of the urban population to air pollutants and to inform about the approaches in air quality management that are used in different urban environments.

The potential hazards of substances in the ambient environment of developed countries are well known. Epidemiology and toxicology studies have provided information on a multitude of chemicals and other substances producing adverse health effects. This research has enabled the identification of the hazards and the proposal of action plans aimed at reducing the probability of population exposure to high air pollutant concentrations and preventing the most obvious adverse health effects of the exposure.

WHO and other national and international agencies have reviewed and summarized the accumulated evidence on ambient (and indoor) air quality and its health aspects. Of major support to countries in risk assessment and national standard setting have been WHO's Air Quality Guidelines for Europe /10/. Between 1993 and 1996, the guidelines were updated and are presently in press /11/. The Air Quality Guidelines for Europe have recently been made globally applicable in a document entitled *Guidelines for Air Quality* /12/. This document includes guidance derived in the Environmental Health Criteria Series of the International Programme for Chemical Safety (IPCS) and the Inter-Organization Programme for the Sound Management of Chemicals (IOMC). The globally applicable Guidelines for Air Quality document takes into consideration factors that might be influential for the health outcome in developing regions and binds the air quality guidelines into the framework of air quality management.

The present paper is organized as follows. The review first describes the air pollution trends in developed and developing countries as can be inferred from the Healthy Cities AMIS /8/ and a report from the European Environmental Agency /13/. A review is then given of the health effects of the 'classic' air pollutants: sulphur dioxide (SO_2), nitrogen dioxide (NO_2), ozone (O_3), carbon monoxide (CO), suspended particulate matter (SPM), and lead. The paper concentrates on epidemiological studies, which can be used to derive exposure-response relations. Health effects of other inorganic and organic air pollutants are not covered here. With respect to the latter air contaminants, the reader is referred to the recent WHO *Air Quality Guidelines for Europe* /10/, the globally applicable *Guidelines for Air Quality* /11/, the documents of the *Environmental Health Criteria* Series of the International Programme for Chemical Safety (IPCS), and the documents published within the Inter-Organization Programme for the Sound Management of Chemicals (IOMC). Finally, the paper gives an outlook on the way forward in the Conclusions and Recommendations section.

AIR POLLUTION TRENDS IN DEVELOPED AND DEVELOPING COUNTRIES

Air Pollution Levels and Trends in Developed Countries

The air pollution indicators in the cities of European countries surveyed in the Dobric Report /13/ include three major air pollution situations.

1. Winter-type smog, due to SO_2 and SPM (as measured by the black smoke (BS) or gravimetric methods).
2. Summer-type smog, due to O_3 resulting from emissions of volatile organic compounds (VOCs) and nitrogen oxides.
3. High annual average concentration levels (including benzene, benzo[a]pyrene (BaP), and lead, in addition to SO_2 and SPM).

According to the estimates in this report, in 70% to 80% of all surveyed cities of more than 500,000 inhabitants, concentrations exceeded the 1987 air quality guidelines of WHO during episodes of winter-type smog. In about 28% of cities, concentrations around or higher than twice the WHO guidelines have been observed during days with poor dispersion conditions. Higher SPM concentrations dominated in most the cities.

In summer-type smog, the produced O_3 will be found downwind of the area of emissions. An exception is when cities are located in confined valleys, or when the air is trapped by special meteorological conditions for significant photo-oxidation to take place. Examples of such cities where high O_3 concentrations go up to 400 μ/m^3, include Athens, Barcelona and Los Angeles.

Urban street pollution is monitored in many cities, and the measurements show that short-term maximum concentrations of CO, NO_2, and SPM may exceed air quality guidelines or standards by a factor 2 to 4, depending on the actual traffic and dispersion conditions of the street. In Europe, between 9 and 18 million people are exposed to these high concentrations. Road transport is the significant source of smog occurrences and long-term average concentrations of compounds such as lead, benzene, SPM, and BaP. Road transport contributes on average of more than half to the NO_2 concentrations and about 40% to the VOC concentrations. In many cities, the road traffic contribution to pollution by these compounds is even higher. All these combustion processes in road traffic produce fine (less than 2.5 μm aerodynamic diameter) and ultrafine particles (less than 0.1 μm aerodynamic diameter).

While NO_2 emissions from stationary sources have decreased in many urban areas, emissions from motor vehicles have increased. The latter is due to the growth in the number of vehicles and the distance traveled per vehicle, both of which have a larger impact than the reduction in emission factors. As a consequence, urban NO_2 concentrations did not decrease but rather remained constant or were slightly increasing.

Through substitution of coal and heavy fuel oils by cleaner fuels, such as gas oil and natural gas, and by electricity and heat supplied from large electric power plants and district heating plants, many cities have considerably improved their local air quality in recent decades. Emission controls have been particularly successful in reducing SO_2, dust, and fly ash emissions to the atmosphere and in reducing the emissions of various gases from the process industries.

Air Pollution Levels and Trends in Developing Countries

In a recent publication /14/, the air pollution situation of cities in developing countries was analyzed. The observations reported there are based on the data collected in the database of the Healthy Cities AMIS /6, 7/. In most of the 100 cities presented in this database, the annual mean concentrations of SO_2 in residential areas did exceed 50 $\mu g/m^3$. Noticeable exceptions are several cities in China, with an SO_2 concentration of 330 $\mu g/m^3$ in Chongqing and 100 $\mu g/m^3$ in Beijing in 1994. High levels of SO_2 may also be seen in other developing countries, especially in those with cold winters. Daily mean concentrations of SO_2 in the centre of Kathmandu valley, Nepal, were around 200 $\mu g/m^3$ /15/. In monitoring sites close to main

roads, the reported range of 310 to 875 $\mu g/m^3$ reflects the influence of emissions from traffic.

In most cities with data allowing trend assessment, a decline in the mean annual SO_2 concentration was seen over the 1990s. The most dramatic reduction of air pollution with SO_2 was reported from Mexico City, where the concentration in various residential areas dropped from over 100 $\mu g/m^3$ in 1990/1991 to less than 40 $\mu g/m^3$ in 1995/1996. In the most polluted Chinese cities, an annual decline rate was between 1% and 10%.

With respect to SPM, the most commonly reported indicator is the mass of total suspended particles (TSP). In most of the cities, the TSP annual mean concentration exceeds 100 $\mu g/m^3$, with the levels exceeding 300 $\mu g/m^3$ in several cities of China and India /7/ and 200 $\mu g/m^3$in the Kathmandu valley in 1995 /15/. No overall systematic and significant change in TSP levels is evident in most cities. Nonetheless, a decrease in TSP concentration in Mexico City is consistently observed. In some Chinese cities the opposite tendency can be seen. In Guangzhou, for example, the data show a most rapid increase in TSP concentrations from less than 150 $\mu g/m^3$ in 1990/1992 to more than 300 $\mu g/m^3$ in more recent years.

According to the AMIS database, the mass concentration of particles with aerodynamic diameter less than 10 μm (PM_{10}) is also measured in a limited number of cities. The annual average PM_{10} levels ranged from 50 to 100 $\mu g/m^3$ in the years 1995/1996. The highest concentrations, exceeding 250 $\mu g/m^3$, were observed in Calcutta and New Delhi, India. In most cities, an increase of the PM_{10} concentration was seen in the 1990s, occurring even when a decrement in TSP was reported. An opposite trend and a decrement in PM_{10} level were seen in cities of Central and South America. In Mexico City, the relative decrement in PM_{10} was faster than that of TSP.

In most cities reporting to AMIS, the annual mean concentration of NO_2 remains moderate or low, not exceeding 40 $\mu g/m^3$. In Mexico City, Mexico and Cape Town, South Africa, however, the annual average of 70 $\mu g/m^3$ was exceeded regularly in the 1990s. Data from monitors in central Sao Paulo, Brazil indicate an annual mean of 240 $\mu g/m^3$ in 1990/1991 /16/. The trends vary between the cities, but a 5% to 10% annual increase was more common than a decrease in concentration of this pollutant. The highest NO_2 levels and the increasing trends are observed in cities with high and increasing car traffic. In South Asia or in Latin America, such high NO_2 concentrations, combined with the intensive UV radiation, results in photochemical smog with high O_3 concentrations. This is illustrated by the analysis of temporal and spatial patterns of tropospheric O_3 in New Delhi, India /17/. Here the build-up of O_3 over the day is faster than the scavenging of O_3 by NO_2. The mixture of high NO_2 emissions from gasoline combustion with the intensity of UV in Mexico City is the cause of photochemical smog in that city as well. In 1994 to1996, O_3 concentrations exceeded the WHO air quality guideline for over 300 days per year, and the 95th percentile of the maximum daily 1-hour average O_3 concentration was around 500 $\mu g/m^3$. The Mexican 8-hour O_3 standard is also exceeded on most days of the year. Krzyzanowski and Schwela /14/ stated that in many cities of developing countries, the reported concentrations of air pollution reach levels of concern for public health.

CLASSIFICATION OF HEALTH EFFECTS OF AIR POLLUTANTS ON THE VARIOUS COMPARTMENTS OF THE HUMAN BODY

The health impacts of air pollutants are manifold and can become manifest in any compartment of the human body. The compartments affected include the respiratory system, the immune system, the skin and mucous

tissues, the sensory system, the central and peripheral nervous system, and the cardiovascular system.

The health effects of air pollution on the respiratory system (lower airways) include acute and chronic changes in pulmonary function, increased incidence and prevalence of respiratory symptoms, sensitization of airways to allergens, and exacerbation of respiratory infections, such as rhinitis, sinusitis, pneumonia, alveolitis, and legionnaires' disease. Principal agents for these health effects are the combustion products SO_2, NO_2, SPM having a mean aerodynamic diameter below 10 μm and smaller, and CO. In addition indoor air pollutants, fine SPM, formaldehyde, and infectious organisms can also act as important agents.

The health effects of air pollution on immune system allergies manifest themselves in the exacerbation of allergic asthma, allergic rhinoconjunctivitis, extrinsic allergic alveolitis/hypersensitivity pneumonitis. In sensitized individuals, such effects can produce permanent lung damage including pulmonary insufficiency. Principal agents are outdoor allergens and indoor air agents such as house dust mites, cockroaches, organisms living in the pelt of pets, insects, and molds in high humidity environments. Multicenter studies have shown different patterns of allergic disease (for example, asthma, rhinitis, eczema) as well as allergic hypersensitization. Such variations cannot be reconciled by geographical differences in allergen exposure because the major aeroallergens are widespread, implying a variable susceptibility of different populations to allergic disease. In Europe the prevalence of allergic diseases is highest among children and young adults. There are significant differences in the prevalence of hay fever and asthma between Eastern and Western Europe /18/.

The health effects of air pollution on the skin and on mucous tissues (eyes, nose, throat) are mostly irritations. Primary sensory irritations include a dry, sore throat, a tingling sensation of nose, and watering and painful eyes. Secondary irritation is characterized by edema and inflammation of the skin and mucous membranes up to irreversible changes in these organs. Principal agents include VOCs, formaldehyde and other aldehydes (for example, acetaldehyde, acrolein), and environmental tobacco smoke.

The sensory effects of air pollution include nuisance and annoyance reactions caused by the perception of air pollutants through sensory organs. Volatile organic compounds, formaldehyde, and environmental tobacco smoke can act as principal agents.

The effects of air pollution on the central nervous system (CNS) manifest themselves in damage to nerve cells, either toxic or hypoxic/anoxic. Principal Agents are VOCs (acetone, benzene, toluene, formaldehyde), CO, and pesticides. In infants and young children, neurophysiological changes caused by lead can result in developmental retardation and irreversible deficiencies.

The effects of air pollution on the cardiovascular system develop through reduced oxygenation and result in increased incidence and prevalence of cardiovascular disease, myocardial infarction, and a consequent increase in mortality from cardiovascular disease. Principal agents are CO, SPM, and environmental tobacco smoke.

The carcinogenic effects of air pollution are associated with lung cancer, skin cancer, and leukemia. Principal agents for lung cancer have been identified as arsenic, asbestos fibers, chromium, nickel, cadmium, polycyclic aromatic hydrocarbons, trichloroethylene, environmental tobacco smoke, and radon. Benzene is known to produce leukemia, and ultraviolet radiation is a causative agent of skin cancer. A difficult question is that of synergism among the different carcinogenic compounds and between carcinogenic and non-carcinogenic agents. The question

of synergism is largely unresolved. Also other carcinogenic effects might also exist but are not well assessed.

HEALTH EFFECTS OF 'CLASSIC' AIR POLLUTANTS

Sulphur Dioxide

Sulphur dioxide (SO_2) is a colorless gas that is readily soluble in water. Natural sources, such as volcanoes, contribute to environmental levels of SO_2. Man-made contributions include the use of sulphur-containing fossil fuels for domestic heating and for power generation. Annual mean concentrations of SO_2 in major European and American cities are now largely below 100 $\mu g/m^3$. Daily mean concentrations are below 500 $\mu g/m^3$.

The toxicological and epidemiological literature through 1996 on the health effects of SO_2 was reviewed during the process of updating and revising the air quality guidelines for Europe /11/. Another review was published in 1996 by a Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society /19/. One very recent review /20/ describes the health effects of SO_2 arising from traffic pollution and in another, the toxicology of SO_2 is reviewed by Schlesinger /21/. The review presented here concentrates mainly on epidemiological findings and is based on previous reviews /11, 20/ and other recent publications on the health effects of SO_2.

Most information on the acute effects of SO_2 comes from controlled chamber experiments on volunteers exposed to SO_2 concentrations above 500 $\mu g/m^3$ for periods ranging from a few minutes up to a few hours /11/. Normal healthy individuals show upper respiratory symptoms, whereas asthmatics and persons with respiratory hyper-reactivity exhibit acute responses. Acute responses occur within the first few minutes after commencement of inhalation. The effects in sensible individuals include reductions in mean FEV_1, reductions in forced vital capacity (FVC), increases in specific airway resistance, and symptoms, such as wheezing or shortness of breath. These effects are enhanced by exercise that increases the volume of air inspired, as it allows SO_2 to penetrate further into the respiratory tract.

Time-series studies in Athens and in two French cities indicate that SO_2 has independent (from other measured pollutants) acute adverse health effects on daily mortality for males and females in the age group of 65 yr and over /22, 23/. A study in Mumbai, India also showed effects of SO_2 on the daily mortality from cardiorespiratory diseases, but the data were insufficient to isolate either the separate or the combined effects of SO_2 and SPM /24/. In a Chinese study in Beijing /25/, a highly significant association was found between logarithmic levels of air SO_2 and the daily number of deaths, adjusted for the influence of temperature and humidity. The stronger effects were seen on deaths caused by chronic bronchitis, chronic obstructive pulmonary disease, and cor pulmonale. Unfortunately, the results of all these studies cannot be used for calculating dose-response relations.

In a study in Crakow, Poland /26/, significant but small correlations were observed during winter months between mortality of male people over 65 years of age and SO_2 and PM_{20} (suspended particulate matter of mean aerodynamic diameter below 20 μm), respectively. After adjustment for SO_2 levels, PM_{20} had no additional effect on mortality. The authors estimated that with an increase of SO_2 concentration of 100 $\mu g/m^3$, the daily number of deaths from respiratory system diseases increased by 19% and deaths from circulatory system diseases by 10%. Several studies, including those of the APHEA project, showed a significant increase in total mortality, cardiovascular mortality, and respiratory mortality with increased SO_2 /27–35/. Certain studies included

the analysis of the influence of other compounds in the air pollutant mix and meteorological variables /27–30/. In the APHEA studies, however, multi-pollutant models were not applied /31–35/. Other recent studies could not establish a significant increase in total mortality with increased SO_2 in the presence of other pollutants, except under special seasonal conditions /36–40/. In a multivariate study in the Netherlands, the relatively low SO_2 concentrations do not seem to have any short term effect on mortality /41/, although on a 1-pollutant basis a significant correlation was found between SO_2 and mortality.

With respect to morbidity (hospital admissions for cardiovascular or respiratory diseases), an increase in SO_2 was significantly associated with an increase in adverse health effects, even when other pollutants were considered /42, 43/. Within the APHEA project, however, most other studies did not give significant results /11/.

Also with respect to lung function parameters, a wide range of sensitivity has been demonstrated, both among normal subjects and among those with asthma (for example, Nowak et al. /44/). People with asthma are the most sensitive group in the community. In an Austrian study /45/, increased SO_2, NO_2, and O_3 were significantly associated with decrements of FEV_1. A French study in six cities /46/ reported that in both adults and children the higher the SO_2 concentration, the lower the FEV_1. Continuous exposure-response relations, without any clearly defined threshold, are evident. An example of an exposure-response relation for asthmatic patients is shown in Fig. 1, expressed in terms of change in FEV_1 after a 15-min exposure /12, 47/. In a recent cross-sectional study of adults in Switzerland a consistent and significant association between SO_2 and FEV_1 and FVC was found, although such an association also existed with NO_2 and PM_{10}. The influence of individual compounds was not separated in a multi-pollutant model /48/.

Nitrogen Dioxide

Nitrogen dioxide (NO_2) is a reddish-brown gas with strong oxidant properties. Natural background concentrations are low compared with concentrations in urban areas. Annual mean NO_2 concentrations in urban areas throughout the world range between 20 and 90 $\mu g/m^3$. Highest 1-hour averages amount

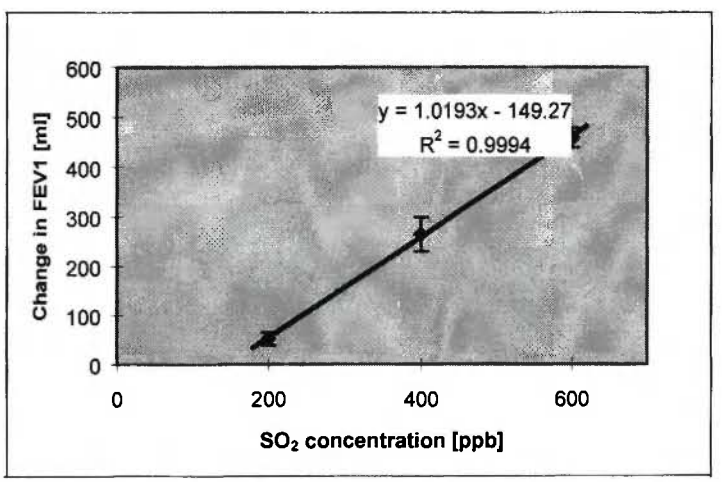

Fig. 1: Mean change of FEV_1 in asthmatics with changing SO_2 concentrations (WHO 1999b)

up to 1000 $\mu g/m^3$. High levels of NO_2 of the order of 200 $\mu g/m^3$ during several days have been observed in homes with unvented combustion devices. Even higher values in the mg/m^3 region have been estimated for indoor skating rinks. Such exposures are related to the use of gasoline-powered ice resurfacing machines /49/.

Most effects of NO_2 are exerted in the airways and the lung. The health effects of NO_2 have been recently reviewed in various studies /11, 20, 50–54/. The World Health Organization /11/ reviewed available data from animal toxicology experiments, findings from controlled studies, and from epidemiological studies. Hazucha /52/ concentrated on controlled exposure studies, whereas Ackermann-Liebrich and Rapp /53/ and Chauhan et al. /54/, reviewed epidemiological studies of indoor and outdoor exposure to NO_2.

Nitrogen dioxide increases bronchial reactivity, as measured by the response of normal and asthmatic subjects following exposure to pharmacological bronchoconstrictor agents, even at levels that do not affect pulmonary function directly in the absence of a bronchoconstrictor. Some, but not all, studies show increased responsiveness to bronchoconstrictors at NO_2 levels as low as 376 to 565 $\mu g/m^3$; other studies found that higher levels had no such effect. Therefore, a consistent evaluation of the health consequences of the increased responsiveness to bronchoconstrictors is not yet possible /11/. Recent studies have shown an increased reactivity to natural allergens in the same concentration range. The results of repetitive exposures of such individuals, or the impact of single exposures on more severe asthmatics, are not known /11/.

A meta-analysis of studies conducted among children of school-age suggested that the use of gas for cooking with an equivalent exposure to 30 $\mu g/m^3$ was associated with a slight, but significant, 20% increase in the prevalence of respiratory illness /55/. Studies among infants, however, have failed to show this association /56, 57/. Other studies suggested that gas cooking was consistently related to respiratory symptoms and decrement in lung function suggestive of asthma, in adults /58–60/. An analysis within the European Community Health Survey, however, has shown that the association between gas cooking and symptoms and lung function is not consistently observed among females in all populations /61/. In these studies, NO_2 concentrations were not measured. Exposure to higher NO_2 concentrations in Australia have indicated associations between exposure of children and the incidence of asthma, wheezing, colds, sore throats and school absenteeism /62, 63/.

Three other studies have shown that NO_2 at levels of several hundred micrograms per cubic meter can slightly affect the specific airway response of persons with asthma to inhaled allergens /64–66/. A recent study on air pollution and acute asthma in Southern Sweden has suggested that aggravation of asthma is related to daily variations in NO_2 /67/.

Several studies have detected significant associations between NO_2 exposure and respiratory symptoms /68–70/, including a study of increased emergency department visits of patients with symptom exacerbation of chronic bronchitis and emphysema /71/. Other studies could not establish such associations /72, 73/.

The results of a number of outdoor studies consistently indicate that children with long-term ambient NO_2 exposures exhibit increased respiratory symptoms of longer duration /74/, show a decrease in lung function /68/, and an increase of the incidence of chronic cough, bronchitis and conjunctivitis /75/. Outdoor NO_2 epidemiological studies, however, as with indoor studies, provide little evidence that long-term ambient NO_2 exposure is associated with health effects in adults /11/.

Although none of the available studies yields confident estimates of long-term exposure-effect levels in adults, the available results most clearly suggest respiratory effects in children at annual average NO_2 concentrations in the range of 50 to 75 $\mu g/m^3$ or higher /11/.

In panel cohort studies, the associations of outdoor NO_2 to respiratory symptoms and lung function decrements in children were investigated. Only one study found associations with increases of cough and lower respiratory symptoms in single-pollutant analysis /76/ which, however, disappeared when PM_{10} was included. Other studies found associations only to lung function parameters /77–80/.

Long-term studies on the associations between ambient NO_2 exposure and the respiratory health of adults are relatively few. Increasing respiratory symptoms, such as chronic obstructive pulmonary diseases, cough, wheezing, phlegm were observed /81, 82/, as well as decreases in lung function parameters /48, 83, 84/. In some cases, however, separating the influence of NO_2 from that of the other pollutants has not been possible.

In time-series studies, associations of ambient NO_2 were found between increase of peak-hour NO_2 concentrations and total daily mortality /30, 32, 40; 85–87/; in some studies associations between NO_2 exposure and cardiovascular mortality was also suggested /32, 40/. The problem of separating the influence of NO_2 on daily mortality from that of other pollutants has, however, weakened the power of the analysis /87/. Similar studies on the association between NO_2 exposure and hospital admissions have not yielded consistent results /53/, mostly because other pollutants, such as CO and SPM, exhibited a stronger association than did NO_2.

In conclusion, there is still not enough evidence from epidemiological studies for a causal relation between NO_2 and the observed health effects /53/ or for constructing consistent quantitative exposure-response relations /11/. From the existing evidence it can, however, be concluded that NO_2 contributes to the health effects observed.

Carbon Monoxide

Carbon monoxide (CO) is a colorless, odorless and tasteless gas that is relatively poorly soluble in water. Anthropogenic emissions of CO originate primarily from the incomplete combustion of carbonaceous materials. The largest proportion of such emissions is produced as exhausts of internal combustion engines, especially of vehicles with petrol engines. The ambient concentrations in urban areas depend largely on the density of vehicles. In most cities, therefore, the highest 1-hour concentrations occur in the morning and evening rush-hours. In the streets of large European cities, the 8-hour average CO concentrations are generally between 1 and 20 mg/m^3 /88, 89/. In such areas, the concentrations measured inside vehicles are, in general, two-to-eight times higher than those measured in the ambient air /90–93/. Among other factors, traffic patterns, car models, ventilation conditions, car maintenance and season affect CO levels inside cars /94–96/. Measurements of CO at fixed-site monitoring stations seem to underestimate the 1-hour exposures of various urban population groups /97–99/. Such measurements, however, may reflect better population exposure at 8-hour exposures /97, 98, 100/. In environments with insufficient ventilation (such as tunnels, car parks, and so forth), CO levels may be much higher than common ambient levels /101, 102/. In indoor ice arenas and arenas of indoor motor shows, very high CO concentrations of between 2 and 150 mg/m^3 as 1-hour averages frequently occur /103–105/. Even acute CO poisonings have been observed in ice arenas /106, 107/. Environmental tobacco smoke in indoor environments can raise 8-hour CO

concentrations to 50 mg/m^3 /108/.

The lungs are the only significant route for CO uptake from the environment. Carbon monoxide diffuses rapidly across alveolar, capillary and placental membranes. Approximately 80% to 90% of absorbed CO binds with hemoglobin to form carboxyhemoglobin (COHb), which reduces the oxygen-carrying capacity of the blood and impairs the release of oxygen from hemoglobin. The uptake and elimination of CO is often described by the Coburn-Foster-Kane exponential equation /109, 110/. During exposure to a fixed concentration of CO, the COHb concentration increases rapidly at the onset of exposure, and starts to level off after 3 hours. After 6 to 8 hours of exposure, concentrations in alveolar breath and ambient air become practically equal.

The health effects of CO were reviewed in several papers /11, 19, 20, 111/. The most recent study was published in the Environmental Health Criteria Series of the WHO /110/. Severe hypoxia from acute CO poisoning may cause both reversible, short-lasting, neurological deficits and severe, often delayed, neurological damage. The neurobehavioral effects include impaired coordination, tracking, driving ability, vigilance, and cognitive performance at COHb levels between 5% to 8% (cf. /11/). Behavioural effects of CO exposure, such as vision impairment, have been found to start at COHb levels above 18%, as shown by Benignus /112/.

The pregnant mother, the fetus, and the newborn infant are at high risk of adverse health effects from CO exposures. During pregnancy, maternal COHb levels are usually about 20% higher than the non-pregnant values; fetal COHb levels are as much as 10% to 15% higher than the maternal COHb levels /108/.

Endogenous production of CO results in COHb levels of 0.4% to 0.7% in healthy subjects. During pregnancy, elevated maternal COHb levels of 0.7% to 2.5% have been reported, which are primarily due to increased endogenous production. The COHb levels in non-smoking general populations are usually 0.5% to 1.5%, due to endogenous production and environmental exposures. Non-smoking persons in certain occupations (automobile drivers, policemen, traffic wardens, garage and tunnel workers, firemen, and so on) can have long-term COHb levels of up to 5%, and heavy cigarette smokers have COHb levels of up to 10% /11/. Well-trained subjects engaging in heavy exercise in polluted indoor environments can quickly increase their COHb levels by up to 10% to 20%.

Cardiovascular responses to exercise under low-level CO exposures have been investigated in healthy subjects and in patients with ischemic heart disease and reviewed in several studies /19, 108/. In apparently healthy subjects, the maximal exercise performance decreases at COHb levels as low as 5%. The regression between the percentage decrease in maximal oxygen consumption and the percentage increase in COHb concentration appears to be linear, with a fall in oxygen consumption of approximately 1% for each 1% rise in COHb level above 4%. Post-exposure COHb levels of 2.9% to 5.9% have been associated with a significant shortening in the time to onset of angina, with increased electrocardiographic changes and with impaired left ventricular function during exercise /19, 108/. In addition, ventricular arrhythmias may be increased significantly at a mean post-exercise COHb level of 5% /113/. Epidemiological and clinical data indicate that CO from smoking and environmental or occupational exposures may contribute to cardiovascular mortality and to the early course of myocardial infarction /11, 108/.

A number of studies have investigated the association between CO exposure and daily mortality and hospital admissions due to cardiovascular diseases. An early study by Hexter and Goldsmith /114/ found a positive significant

association between CO and mortality in Los Angeles. More recent studies in Los Angeles established an association between daily mortality and CO, total hydrocarbons, and particulate matter /115/ and CO, NO_2, and particulate matter /85/. These studies, however, noted the strong correlation among the three respective pollutants and could not separate their individual influences. In later studies, no relation was found between CO and daily mortality in Los Angeles, or in Chicago, after adjustment for PM_{10} /116–118/. No relation between CO and daily mortality, with or without adjustment for other pollutants, was found in Amsterdam /38/, and in Sao Paulo, no association could be established between CO exposure and the daily mortality of either children /119/ or adults /16/. In a similar investigation in Philadelphia /120/, such an association was not found either. Other studies did establish an association between CO exposure and daily mortality /121, 122/. Four other studies /27, 30, 31, 123/ showed small, statistically significant relations between CO and daily mortality. Other pollutants and environmental variables, however, were also significant. A detailed discussion of the findings of the studies up to 1995 is provided by Schwartz /124/. He raised the question of whether the demonstrated asso-ciation was causal and asked whether CO might be acting as a proxy for particulate matter.

Recent studies on an association between CO exposure and hospital admissions for cardiovascular disease, especially for persons older than 65 years, were performed in the U.S. /125–127/; in Canada /128/, and in Greece /129/. These studies show that the association between ambient CO and mortality and hospital admissions from cardiovascular disease persists even at very low CO levels, indicating no threshold for the onset of these effects. The study of Morris and Naumova /126/ also showed that the effect of CO on hospital admissions was temperature-dependent, with the magnitude of the effect increasing with decreasing temperature. Ambient CO has been suggested to have more serious health consequences than COHb formation, and at levels lower than that mediated through elevated COHb levels /110, 130/. An extensive interpretation of all these findings is given in /110/.

Ozone and Other Photochemical Oxidants

Ozone (O_3) is a strong oxidizing agent. In the troposphere O_3 is formed through a complex series of reactions of nitrogen oxides and hydrocarbons under the influence of sunlight. Elevated O_3 concentrations of several hundred micrograms per cubic meter have been measured in rural and urban areas. In certain parts of Europe and the U.S., 1-hour mean O_3 concentrations occasionally exceed 350 $\mu g/m^3$. This level is frequently exceeded in Athens, Barcelona, Los Angeles, Mexico City /7/.

The only uptake route of O_3 and related oxidants is inhalation. In humans, the total respiratory tract uptake is 80% to 95%, the efficiency being inversely proportional to flow rates and directly proportional to tidal volumes /12/. Uptake is essentially similar during either the nasal or oral airways (although slightly higher during oral breathing), and the respiratory responses are similar /131, 132/. The health effects of O_3 were recently reviewed in various reports /11, 19, 20, 132, 133/.

Short-term acute effects of O_3 include pulmonary function decrements, increased airway responsiveness and airway inflammation, aggravation of pre-existing respiratory diseases such as asthma, increases in daily hospital admissions and emergency department visits for respiratory causes, and excess mortality /1, 50, 134/. In healthy subjects, after 1 to 3 hours of O_3 exposure during moderate-to-heavy exercise, pulmonary function changes were found for FEV_1 and

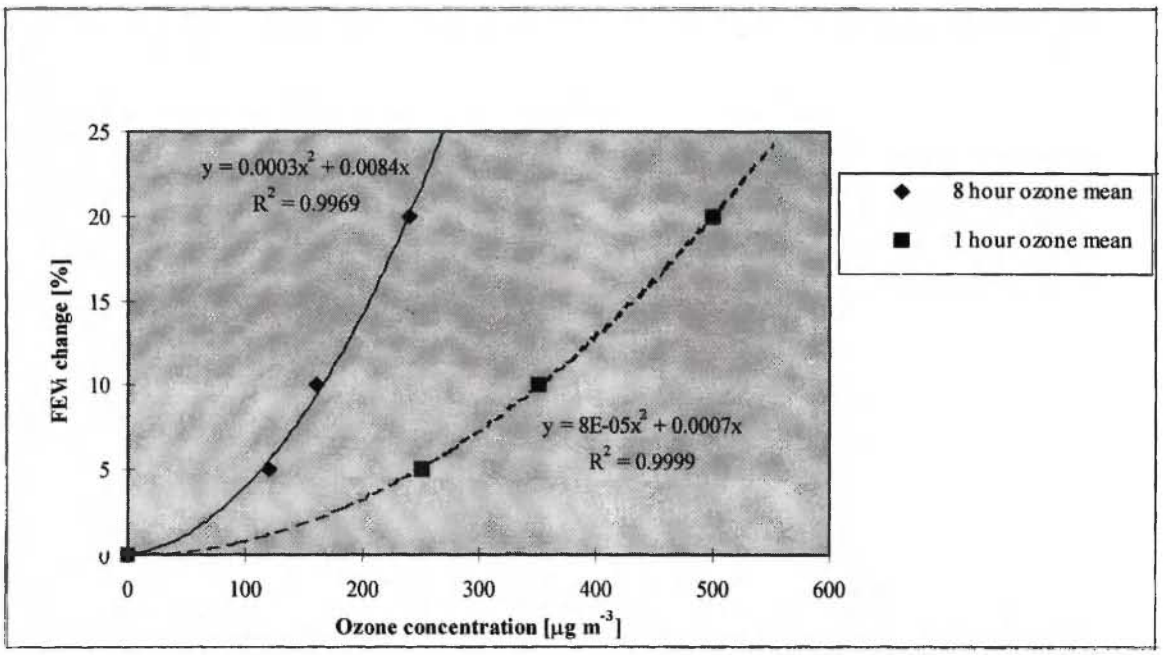

Fig. 2: Change in FEV_1 as a function of O_3 concentration in the most sensitive 10% of active young adults and children.

FVC, airway resistance, and respiratory frequency /1, 50, 134/ For FEV_1, the relations are depicted in Fig. 2, relating to 1-hour and 8-hour exposures, respectively (12, 135). The decrease in FEV_1 is statistically significant at 160 $\mu g/m^3$ for about 6 hours of exposure in a group of healthy exercising adults, with the most sensitive subjects experiencing a more than 10% functional decrease within 4 to 5 hours. Controlled exposure of heavily exercising adults, or children to an O_3 concentration of 240 $\mu g/m^3$ for 2 hours, also produced decreases in pulmonary function /136/. There is no question that substantial acute adverse effects occur during exercise with 1-hour exposure to concentrations of 500 $\mu g/m^3$ or higher, particularly in susceptible individuals or subgroups.

Figure 3 is another example of a non-linear relation between O_3 levels and an adverse health outcome, namely, change in the inflammatory response of young adults exercising outdoors (neutrophil influx in lungs of healthy young adults exercising outdoors at more than 40 L/min expiratory volume in the lung /1/. The dose-response relations in these figures represent expert judgment, based on the collective evidence from numerous studies and linear extrapolation in a few cases in which data were limited. Interestingly, these dose-response relations appear to be non-linear. It should be kept in mind that such relations have an uncertainty region that is characterized by the 95% confidence intervals.

Respiratory symptoms, especially coughing, have been associated with O_3 concentrations as low as 300 $\mu g/m^3$. Ozone exposure has also been reported to be associated with increased respiratory hospital admissions and the exacerbation of asthma. Such effects are observed with exposures to ambient O_3 (and co-pollutants) and with controlled exposures to O_3 alone, demonstrating that most functional and symptomatic responses can be attributed to O_3.

In several studies, daily mortality was significantly associated with various O_3 measures in

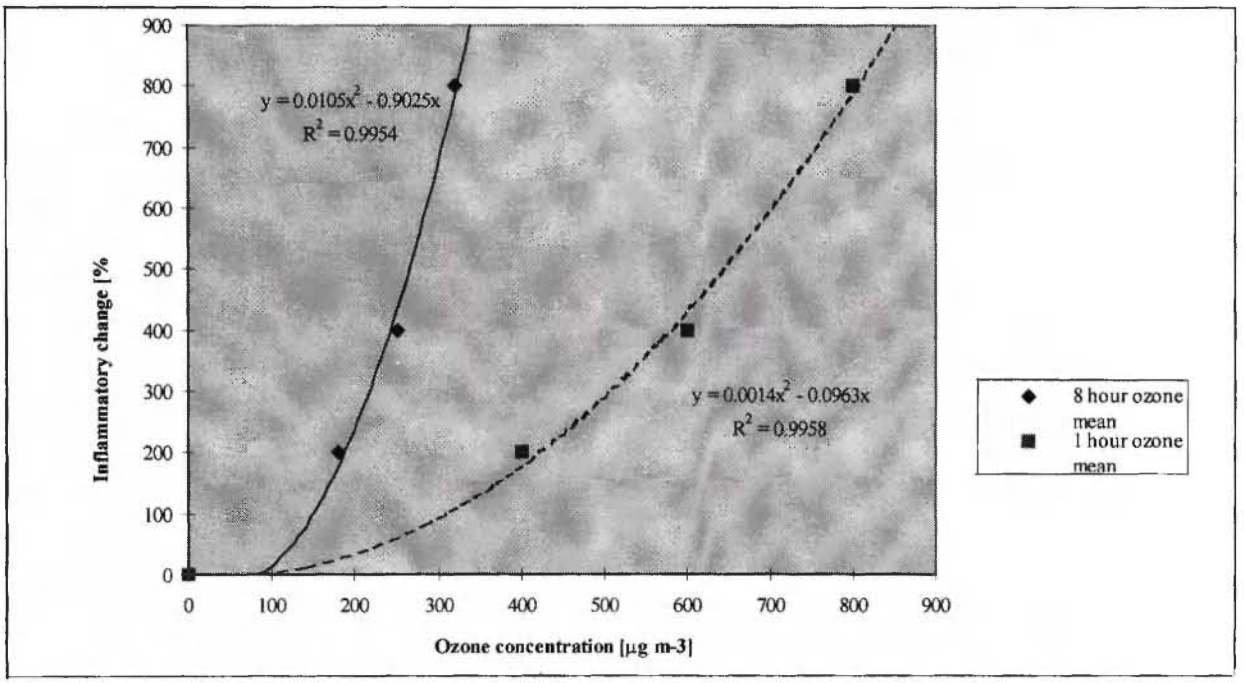

Fig. 3: Inflammatory change as a function of O_3 concentration.

Philadelphia /120, 137/, London /40/, Cook County, Illinois /118/, Rotterdam /138/; in four cities of the APHEA project: Athens, Barcelona, London, Paris /87/; in 11 Canadian cities /121/. The association between daily mortality and O_3 levels remained significant even when other pollutants and con-founding variables were included. In three other studies investigating the association between air pollution and daily mortality, in multi-pollutant models, no significant influence of O_3 levels was found in Mexico City /139, 140/ and Rome /141/. In Mexico City a significant influence of O_3 disappeared when total SPM and SO_2 were included simultaneously to O_3. In a synthesis analysis of seven studies using a non-linear temperature, a relative risk for a daily mortality of 1.056 per 100 ppb increase in daily1-hour maximum O_3 was estimated /133/. The association between O_3 levels and hospital admissions were recently reviewed by the U.S. Environmental Protection Agency (US EPA) /132/ and by Thurston and Ito /133/. On the basis of the US EPA report, associations (depicted in Fig. 4) between daily hospital admissions for respiratory diseases and O_3 levels were developed /11, 12/. These relations summarize the associations found in various U.S. and Canadian studies performed before 1993 /142, 143/. Later studies also found significant associations between asthma and total respiratory admissions in Toronto, Ontario /128, 144, 145/. In a multi-pollutant study of hospital admissions for respiratory diseases a clear and statistically significant association between O_3 and hospital admissions in Toronto, Ontario, and the effect of SPM was greatly reduced in the multi-pollutant model /146/. In five out of six U.S. cities (Birmingham, Alabama; Minneapolis-St. Paul, Minnesota; Spokane, Washington; New Haven, Connecticut; Detroit, Michigan; and Tacoma, Washington), O_3 was positively and significantly associated with pneumonia and COPD admissions (147–151/. In another study of an extended set of.

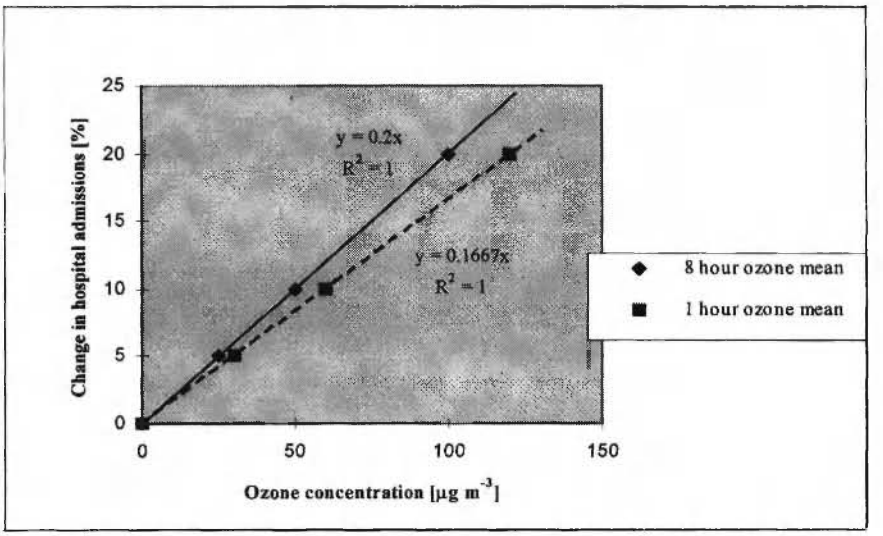

Fig. 4: Increase in hospital admissions for respiratory conditions as a function of O_3 concentration

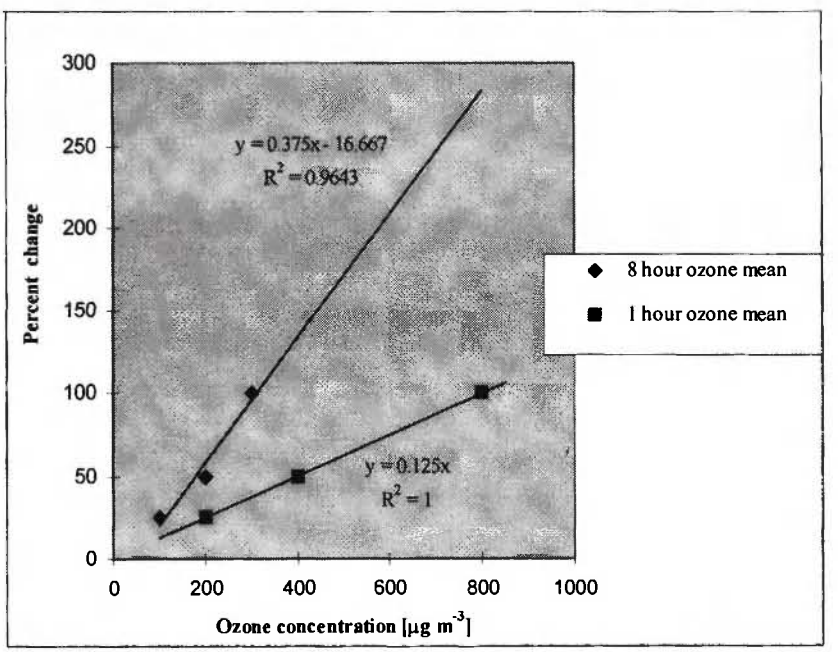

Fig. 5: Change in symptom exacerbation among adults and asthmatics as a function of O_3 concentration.