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Health relevance of particulate matter from various sources

Report on a WHO Workshop
Bonn, Germany, 26-27 March 2007

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Regional Office for Europe**

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ABSTRACT

Identification of the physical and chemical characteristics of particulate matter (PM) to determine its toxicity could facilitate targeted abatement policies and more effective control measures to reduce the burden of disease due to air pollution. A WHO workshop evaluated the progress in research on this important issue. The participants concluded that current knowledge does not allow specific quantification of the health effects of emissions from different sources or of individual PM components. It is therefore appropriate that current risk assessment practices consider particles of different sizes, from different sources and with different composition, as equally hazardous to health. The available evidence on the hazardous nature of combustion-related PM (from both mobile and stationary sources), however, is more consistent than for PM from other sources. Better understanding of the role of various characteristics of PM will require better characterization of the population exposure to the source-specific pollution, as well as improvement and widening of the scope of health outcomes studied.

Keywords

AIR POLLUTANTS - adverse effects - toxicity
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Background

The health burden due to particulate matter (PM) air pollution (PM₁₀ and PM_{2.5}) is one of the biggest environmental health concerns in the WHO European Region and around the world. A particularly vexing research challenge has been identifying the physical and chemical characteristics of PM to determine toxicity. This is critical for making links back to the sources of the most hazardous particles, thereby allowing for the design of the most effective risk reduction strategies. Many scientific and policy-making groups have asked about the health relevance of PM from various sources, including: the Clean Air for Europe (CAFÉ) Steering Group, in the framework of preparation of the European Union (EU) air quality strategy; and various bodies working under the United Nations Economic Commission for Europe (UNECE) Convention on Long-range Transboundary Air Pollution, particularly in view of the current review of the Protocol to Abate Acidification, Eutrophication and Ground-level Ozone (the Gothenburg Protocol) to the Convention. The question is also an important priority for research identified by the United States National Academy of Science, and was considered by the WHO working group preparing the recent update of the WHO air quality guidelines.

Intensive research on this important question continues, and further studies are planned. The WHO Regional Office for Europe therefore organized a workshop to enable scientists from various disciplines to exchange views on the health effects of PM from different sources, and particularly to improve health scientists' understanding of the physical and chemical properties of atmospheric PM from various sources and the impact of those properties on population exposures to PM. This knowledge should allow more efficient and focused design of studies on health effects, addressing the most urgent public health questions. In addition, the workshop enabled atmospheric scientists and exposure assessment specialists to evaluate the availability of methods applicable to epidemiological studies, and to discuss the further improvement of exposure assessment methods, the atmospheric monitoring and modelling necessary to increase their usefulness in epidemiological studies and the estimation of the burden of disease related to specific pollution sources. The participants drew conclusions on the current status of research, as well as making recommendations on further studies and the development of methods.

Process

The workshop discussion was based on evidence from recently published or current studies on the health effects of PM that consider its chemical or physical properties and links to specific pollution sources. A recent evaluation of the evidence published by WHO in the 2005 global update of its air quality guidelines¹ also provided background information.

The WHO Regional Office for Europe hosted the workshop at its WHO European Centre for Environment and Health, Bonn. As participants, the Regional Office welcomed 42 experts from 21 countries: experts active in research on health effects of PM, scientists developing methods for exposure assessment, representatives of national authorities involved in assessing and managing the health risks from air pollution and observers from international organizations. Bert Brunekreef and Robert L. Maynard co-chaired the workshop, and Per E. Schwarze and Leendert

¹ *Air quality guidelines – Global update 2005. Particulate matter, ozone, nitrogen dioxide and sulfur dioxide*. Copenhagen, WHO Regional Office for Europe, 2006 (<http://www.euro.who.int/Document/E90038.pdf>, accessed 27 June 2007).

van Bree acted as rapporteurs. The workshop was supported by funds from the German Federal Environment Ministry, which are gratefully acknowledged.

Before the meeting, selected experts were invited to provide a background to the discussion by summarizing their observations and study results on the health relevance of PM from various sources. Their presentations and the subsequent discussion were structured under the headings:

- exposure to PM from various sources;
- assessment of health effects of PM, focusing on specific sources;
- PM size as a health-related parameter;
- chemical characteristics of PM as a health-related parameter; and
- study designs to identify health-relevant PM sources.

Annex 1 gives summaries of the presentations and lists the presenters. The participants are listed in Annex 2.

Discussion

PM is a complex, heterogeneous mixture, whose composition (particle size distribution, chemical characteristics) changes in time and space, and depends on emissions from various sources, atmospheric chemistry and weather conditions. Most of the available studies do not attribute the observed health effects to a particular characteristic of PM. The evidence is most consistent for the association of PM emitted by the major combustion sources, mobile and stationary, with a range of serious health effects, including increased morbidity and mortality from cardiovascular and respiratory conditions. Current knowledge, however, does not allow precise quantification or definitive ranking of the health effects of PM emissions from different sources or of individual PM components. Thus, current risk assessment practices should consider particles of different sizes, from different sources and with different composition as equally hazardous to health. It is also consistent with the WHO air quality guidelines recommendation to use the mass concentration of PM_{2.5} or PM₁₀ as the indicator of health risk. In the future, better understanding of the relative toxicity and health effects of particles from various sources could facilitate targeted abatement policies and more effective control measures to reduce the burden of disease due to air pollution.

Accurate characterization of population exposures to PM from specific sources is a prerequisite for more informative studies of the health effects. Temporal and spatial differentiation of PM composition requires dispersion models with high spatial and temporal resolution, based on reliable emission inventories. The workshop participants, however, noted that such inventories are not available in many countries in the WHO European Region. In addition, existing inventories suffer from gaps in emission data, especially for primary PM. These gaps affect the accuracy of air pollution models and their usefulness for exposure assessments. In addition, the scarcity of monitoring data on component-specific PM concentrations also makes model validation difficult. Analysis of the health effects of high-pollution episodes, often characterized by PM compositions different from those on other days, may help in identifying critical characteristics that reflect differing toxicity. These analyses might profit from the use of back trajectory models identifying contributions of individual PM sources. Such models and other methods of analysis of the fate of PM in the atmosphere may also increase understanding of the changes of toxic properties of PM transported over long distances.

The participants considered a recent overview of the health effects of PM that was published as part of the update of the WHO air quality guidelines, as well as more recent, unpublished research in Europe and the United States of America. New evidence shows that long-term exposure to air pollution not only affects outcomes such as premature deaths but also contributes to the development and progression of subclinical and clinical disease. The attribution of effects to specific PM characteristics remains limited, due to the scarcity of the relevant exposure data. Some results, however, suggest differential toxicity among PM components for a given health endpoint, as well as differences in the affected health endpoints themselves. For example, subchronic studies with animals exposed to concentrated ambient particles show serious cardiopulmonary effects, as well as some unexpected responses in the liver and brain. This highlights the need for future studies to include effects other than those classically studied.

Adverse health outcomes have been associated with various size fractions within the PM₁₀ range. There is some indication that thoracic coarse particles may preferentially affect the airways and lungs, while fine particles may preferentially affect the cardiovascular system. Ultrafine particles (UFP) may also migrate via the lung to other locations, including the liver, spleen, brain, placenta and fetus. Another route of internal exposure is translocation of UFP via the olfactory nerve system to the brain. The health implications of these observations remain unknown.

Toxicological evidence suggests that different chemical characteristics of particles have different relative risks on a per-unit-mass basis. Different characteristics may be associated with different outcomes. Most of the epidemiological findings are based on single pollutant models, so components associated with health outcomes could be indicators of components that are not measured. In addition, disentangling the effects or source of each pollutant can be challenging when several pollutants are highly correlated in the atmosphere. In addition, interpretation can be challenging when pollutants vary in their levels of measurement error.

One of the hypotheses considered on PM's mechanisms of action is the oxidative potential of the particles or specific components. Several *in vitro* studies with collected particle fractions indicate that particles with a higher oxidative potential have a greater ability to deplete antioxidant defences. Transition metals and oxidized organics in PM seem to be involved, with several studies indicating that transition metals increase the hazardousness of PM. PM from traffic sites seems to have high oxidative activity, and emissions from road traffic have been linked with a wide range of health effects, including effects on the cardiovascular and respiratory systems, and on atopic sensitization to allergens in outdoor air. Although secondary inorganic aerosols have less toxic activity when tested under controlled laboratory conditions, epidemiological studies show significant associations of sulfates and nitrates with various health outcomes. In ambient air, this fraction may act as a carrier for other components or as a surrogate for PM emitted from the combustion of sulfur-containing fuels. The use of different markers and surrogates for specific particle sources is important for the understanding of the complex interactions between particles and different health outcomes, as well as early signs of disease. For example, at a local scale, some sources of PM such as traffic may be indicated by correlated gaseous pollutants, such as nitrogen dioxide (NO₂). Not all markers are unique to one source, however, and some sources do not have routinely measured surrogates.

New research programmes focusing on the health effects of PM from various sources are under way at the national and state levels in the United States. The National Particle Component Toxicity Initiative (NPACT), undertaken recently by the Health Effects Institute (HEI), comprises integrated epidemiological and toxicological studies designed to take advantage of the large differences in PM composition across the United States. The NPACT studies use air quality data on specific PM components and characteristics from multiple sites to study effects on

chronic and acute cardiovascular and respiratory disease. Initial results are expected late in 2009 and final results in 2010–2011. The European collaborative project on the health effects of particles from motor-engine exhaust and ambient air pollution (HEPMEAP – <http://www.hepmeap.org>) is a good example of similar study, conducted on a smaller scale, in Europe.

The workshop participants stressed the need for further large-scale studies in the WHO European Region, combining source-specific air quality information, epidemiological studies and toxicological analysis. Further, they agreed that data collection on air quality should include PM speciation and extend to source apportionment. It should also aim at better spatial and temporal resolution in PM exposure assessment. The participants noted that studies evaluating the effects of interventions, such as implementation of pollution control measures or urban planning (so-called accountability studies), could provide important and timely evidence about the effects of PM from specific sources.

Conclusions and recommendations

The public health and regulatory implications of identifying the health effects of exposure to PM from various sources justify a carefully targeted, intensive research programme. It needs to provide better characterization of the population's exposure to source-specific pollution, and improve and widen the range of health outcomes studied. In particular, the participants made the following recommendations on future research.

Exposure assessment

1. Research in this area should:
 - analyse a wide range of PM sources beyond road traffic or heat and power generation, such as local and regional wood burning or desert dust;
 - ensure that the exposure levels used in toxicological studies correspond to the components and levels of exposure experienced by populations and evaluated by epidemiological studies;
 - consider the contributions of different emissions sources to population exposure;
 - consider possible changes in exposure characteristics (level, PM composition, co-pollutants) over time in long-term studies (for example, include assessment of long-term personal exposure);
 - analyse the health effects of high-pollution episodes using back trajectory models, allowing linkage of acute health outcomes with specific pollution sources;
 - include assessment of other pollutants, especially nitrogen oxides (NO_x), in studies of PM related to transport;
 - validate dispersion models used by epidemiological studies and risk assessment procedures;
 - improve the spatial resolution of exposure estimates whenever possible to account for smaller-scale variations in space; and
 - improve personal exposure estimates to replace the use of stationary monitor data in epidemiological studies.

Exposure data collection

2. Gaps in pollutant emission data need to be reduced to allow improved exposure modelling and more precise attribution of the exposure to pollution sources.

3. Air quality monitoring must widen component speciation and allow better source apportionment.
4. Improved exposure assessment and validation of models will require better spatial and temporal resolution of air quality data, linked with better characterization of the pollutants (for example, providing simultaneous data on various PM size fractions based on dichotomous samplers).
5. Easy-to-operate, low-cost instrumentation for PM monitoring, especially for estimating long-term exposures, should be developed.
6. Correct and systematic collection and preservation of materials (filters) should be ensured, allowing retrospective characterization of exposure.

PM characteristics

7. Research should:
 - identify and use different markers and/or surrogates to characterize source-specific PM;
 - identify the contribution of primary and secondary PM components to the total PM mass; and
 - explore the role of various characteristics of ultrafine, fine and coarse thoracic particles that might be responsible for health effects.

Health effects assessment

8. Assessments of health effects should:
 - consider other biological effects in the studies, beyond classically measured mortality or respiratory function and symptoms;
 - develop assessment methods applicable to epidemiological studies of the effects of pollution on various organs and systems; and
 - study the effects of reductions in air pollution components on health improvement.

Study design for Europe

9. Research programmes and funding agencies should:
 - promote an integrated study approach, combining detailed the characterization of exposure, epidemiological observation of effects in populations and toxicological or clinical evaluation of the effects; and
 - expand the application of intervention studies, investigating the effects of air pollution control measures and urban planning on human exposure and on health effects.

Annex 1

PRESENTATIONS

General

Health impact assessment – It matters what toxicity we attribute to different kinds of PM (F. Hurley)

ExternE (Externalities of Energy – <http://www.externe.info>), a research project of the European Commission, experimented with trying to express quantitatively the view held by at least some researchers, that primary particles from traffic, especially diesel particles, may be more hazardous, per $\mu\text{g}/\text{m}^3$, than secondary particles. Moreover, higher toxicity factors were given to sulfates than to nitrates (Bickel & Friedrich, 2005), because of the many epidemiological studies showing associations between sulfates and mortality or morbidity.

The weighting factors for different components of PM were chosen so that the aggregated effect of a ‘typical’ urban mixture was similar to the standard coefficient for mixed urban $\text{PM}_{2.5}$. The estimated effects of current air pollution levels from all sources are therefore similar, whether different kinds of PM are quantified differently, or not. Differential quantification can however lead to different health impact estimates for various policy scenarios and this may affect policy assessment. This is illustrated using results from an evaluation of the air quality strategy in the United Kingdom, focusing on effects of controls on emissions from road transport (<http://www.defra.gov.uk/environment/airquality/publications/stratevaluation/index.htm>), where ExternE weightings were used in sensitivity analyses

While accepting that it is currently not possible to quantify precisely any differences in PM toxicity, some differential quantification is recommended, at least as sensitivity analyses, assuming that the evidence in favour of differential toxicity is at least as strong as the evidence against. It may be unwise to wait until the evidence for differential quantification is compelling. In that context, the weighting factors of ExternE may be seen as a first step, to stimulate discussion.

Exposure to PM from various sources

Assessing long-term source-specific air pollution exposure in SAPALDIA. (S.L.-J. Liu)

The new, ‘hybrid’ model combines the dispersion and land-use modelling approaches. This model exhibits benefits over each of the models when used individually. The dispersion model approach has been used in recent epidemiologic studies to examine health effects of traffic-specific air pollution. However, there has been no study which has extensively evaluated the predictions from modelling using this approach. Recently popular land-use regression models which use actual measurements have not been constructed to be source specific. The SAPALDIA study evaluated total and traffic-specific PM_{10} , $\text{PM}_{2.5}$, NO_2 , and NO_x concentrations predicted by dispersion models against fixed-site measurements in 1990 and 2000. Model predictions were then used to estimate individual subjects’ historical and cumulative exposures by using a temporal trend model. Modelled PM_{10} and NO_2 predicted at least 60% and 80% of the variability in the measured PM_{10} and NO_2 , respectively.

Traffic-specific pollution estimates correlated well with the NO_x measurements, with an R^2 of 0.78 or higher for background sites but lower R^2 values for traffic sites. When compared with the home outdoor NO_2 measurements, the within-city NO_2 modelling error was larger than that between cities. The within-city NO_2 modelling error was reduced by adding geographic information system (GIS) parameters to enhance the spatial resolution and by including the time and meteorological terms to account for temporal variation and temporal-spatial interactions. The conclusion, that the dispersion model well predicted total PM_{10} , NO_x , and NO_2 and traffic-specific pollution at background sites, was made. However, the model under-predicted traffic- NO_x and NO_2 at traffic sites, although this bias can be significantly reduced by adding GIS, time, and meteorological parameters. The dispersion model predictions for PM_{10} are suitable for examining individual exposures and health effects within- and between-cities. The “hybrid” models for NO_2 provide a further powerful tool for testing hypotheses of traffic-related air pollution effects.

PM speciation in Spain (X. Querol Carceller)

A review of the results of PM speciation and source apportionment performed in different Spanish locations (37 sites) from 1999 to 2006 was reported. The data were made up of time-series of levels of PM_{10} , $\text{PM}_{2.5}$ and PM_1 , and of around 60 components of PM, with at least one year of duration at each site. In most cases PM levels increased from background sites towards the curbside sites. Spatial variations were observed for nitrate and sulfate (the first increasing towards the Mediterranean coast, the second in industrial hotspots and in areas with high shipping emission influence). Both mineral matter and OC+EC increase in the traffic hotspots. High relevance is given to the levels of mineral matter, both in PM_{10} and $\text{PM}_{2.5}$. High levels of mineral matter are measured in traffic hotspots because there is an accumulative process of road dust due to the scarce precipitation. In most of Europe this is not occurring because of more frequent washout of dust by rain. African dust accounts for around 10–30 annual exceedances of the PM daily limit value. Its contribution to the annual mean PM_{10} ranges from $1 \mu\text{g}/\text{m}^3$ to $5 \mu\text{g}/\text{m}^3$. Thus, most of mineral dust has an anthropogenic origin, although Saharan dust contribution may have influence on: the annual mean PM levels recorded in some areas of the country, and the annual exceedances of the number of PM_{10} daily limit value. Source apportionment data of a number of sites is shown, indicating that road traffic may represent as a minimum from 30% to 50% of the PM_{10} annual levels in most Spanish cities. Analysis of PM_{10} , $\text{PM}_{2.5}$ and PM_1 levels shows that PM_1 is much less influenced by dust than $\text{PM}_{2.5}$. A list of trace elements is analysed for the study sites giving a concentration range for different environments studied. Levels of Zn, Sb, Ba and Cu are relatively high in traffic hotspots, even when compared with industrial sites. Finally, a summary of results from a study by Rodriguez et al. (2007), on the relationship of $\text{PM}_{2.5}$ mass and number concentration is shown.

Levoglucosan associated with biomass burning in atmospheric aerosols (R.O. Salonen)

Greatly varying biomass combustion sources (e.g. residential heating, agricultural fires, massive natural vegetation fires) have remarkable impacts on air pollution at local, regional and global scales. Three stable monosaccharide anhydride (MA) isomers (levoglucosan, mannosan, galactosan) are formed by pyrolysis of cellulose and appear as the most abundant organic compounds in biomass smoke particles. Their total mass or even the single, most abundant, MA isomer, levoglucosan, can be used as a specific marker of incomplete biomass combustion. With the help of this tracer, it was estimated in the seven-week six-city field campaigns of the PAMCHAR-EU project that about 37% of the Prague wintertime $\text{PM}_{2.5}$ in 2002–2003 originated from biomass combustion, while the corresponding share was only 0.8% of the Athens

summertime PM_{2.5} in 2003 (Saarnio et al., 2006). In the subsequent national PAMCHAR-FINE project, the contributions of biomass combustion to a four-week average PM_{2.5} in Helsinki in 2003–2004 varied from 8% in summer to 25% in spring. During cold winter months this contribution was much higher. Massive vegetation fires in the Russian Federation and other eastern European countries caused parallel increases in levoglucosan, organic carbon and PM_{2.5} concentrations during several weeks in April–May and August 2006. During these episodes, the 24-hour average PM_{2.5} concentration went up to 60 µg/m³ and the hourly concentration up to 180 µg/m³. It is suggested that fine particles originating from incomplete biomass combustion may cause a significant health hazard to the European populations. This requires further research and attention.

Atmospheric modelling of PM components on European scale (S. Tsyro)

The EMEP model calculates regional background concentrations of PM₁₀ and PM_{2.5} and their chemical composition, including seven aerosol components (sulfate, nitrate, ammonium, elemental and organic carbon, mineral dust and sea salt). The model performance was shown to be acceptable for secondary inorganic components, while calculations of carbonaceous aerosols and natural PM are associated with larger uncertainties (as compared with limited observation data). Uncertainties in model results are to a large degree related to uncertainties in emission data, particularly of primary PM. Model results show that PM chemical composition during pollution episodes may be different from the annual mean compositions. Distinction of different PM chemical components in the EMEP model allows allocating sources of PM according to the country of origin (down to 10x10 km²) and to the emission and activity sector. Model calculated emission allocations for PM for individual countries can be found in MSC-W Country Data notes at the EMEP web site (<http://www.emep.int>).

Spatial pattern of source components – Specifically PM in cities: monitoring and modelling (K. Vincent)

Aerosol (PM₁₀, PM_{2.5} and PM₁) was collected at three different site classifications within and nearby Birmingham in the United Kingdom. These included an urban background location at Birmingham city centre, a roadside site near the University and a rural location 20 km west of the city centre. The dichotomous samplers (for PM_{2.5} and PM₁₀) worked in pairs: one sampler of the pair used PTFE filters only and was analysed for major ions and metals; the other used quartz filters only and was analysed for elemental and organic carbon. This allowed a complete speciation of the collected aerosol. Sampling lasted for a total of two years: one year at Birmingham City Centre and six months at the other two locations. The fraction of aerosol existing in the fine size range increased from the roadside to the city centre to urban location. Ammonium salts dominated the fine fraction at each location. Elemental carbon concentrations in the fine fraction were nearly four times higher at the roadside location compared to the rural location. The modelling method to produce maps of PM_{2.5} and PM₁₀ in the United Kingdom was described. Concentrations derived for urban areas were compared with the urban increment used in IIASA's City-delta project.

Assessment of health effects of PM, focusing on specific sources

Heinz Nixdorf Recall Study: Urban air pollution and coronary atherosclerosis (B. Hoffmann)

Long-term exposure to elevated levels of fine PM is linked to an increased risk of cardiovascular events. Uncertainty remains concerning the cardiovascular toxicity of specific sources, especially

traffic as one of the major contributors to urban PM, and to the mechanisms by which the effect on the cardiovascular system is mediated. In the Heinz Nixdorf Recall Study, the relationship of residential traffic exposure and long-term background PM_{2.5} exposure with the prevalence of coronary heart disease (CHD) and the degree of coronary atherosclerosis, the main underlying pathology for CHD, was examined. The Heinz Nixdorf Recall Study is an ongoing prospective cohort study of 4,814 unselected participants living in three large adjacent cities of the highly industrialized Ruhr area in western Germany that started in 2000. Traffic exposure was assessed by residential proximity to a major road (autobahn and federal highways with mean daily vehicle counts of 10,000–130,000). Annual mean PM_{2.5} concentrations were derived from a small-scale dispersion model, using emission data on a scale of 1 km, meteorological and topographic data. We assessed in-depth information on all known and suspected cardiovascular risk factors and sub-clinical as well as clinical cardiovascular disease endpoints. Multivariable logistic regression analysis adjusted for cardiovascular risk factors and background PM_{2.5} revealed an association between residential proximity to major roads (within 150 m) and prevalence of CHD (OR 1.85, 95% CI: 1.21–2.84) with an exposure-response relationship. To evaluate the relationship with sub-clinical atherosclerosis we used the coronary artery calcification score (CAC), measured non-invasively with electron beam computed tomography. Compared to participants living more than 200 m away from a major road, participants living within 50 m had an OR of 1.65 (95% CI: 1.16–2.34) for a high CAC score (above the age- and gender-specific 75th %ile). Background PM_{2.5} concentrations were less consistently associated with a high CAC. These results show that long-term residential traffic exposure is associated with coronary atherosclerosis and CHD.

Multi-pollutant issues in cohort studies from Europe (B. Brunekreef)

In recent years, several studies in Europe have associated within-city contrasts in air pollution with various health endpoints including mortality in cohort studies of adults, and respiratory morbidity in cross-sectional and cohort studies of children. Many of these studies have used NO₂ contrasts as primary exposure variable, which raises the issue of whether such associations are uniquely found for NO₂ per se, or whether NO₂ acts as a surrogate for a complex mixture of combustion pollutants primarily derived from vehicular traffic. Exposure assessment in these studies has been based on dispersion modelling, on data from routine monitoring networks, on stochastic models developed from dedicated spatially resolved monitoring, or some combination of these. The presentation has focussed on recent results from Europe, emphasizing multi-pollutant approaches as well as validity of exposure assessment.

In contrast to NO₂, sulfur dioxide (SO₂) has not been studied much in recent years. Primarily, associations between SO₂ and mortality and hospital admissions continue to be observed in time series studies. However, coefficients for SO₂ have tended to increase over time in keeping with decreases in SO₂ concentrations, suggesting that some co-varying factor may be responsible. Recently, WHO has considerably decreased its air quality guideline for SO₂ primarily on the basis of the experience in Hong Kong Special Administrative Region of China, which showed reduced mortality and morbidity after a step change in SO₂ but not other pollutants. However, it has been suggested that certain unmeasured transition metals may have changed in step with SO₂, and that these may be responsible at least in part for the observed associations with SO₂. This warrants further studies on health effects of low-level SO₂ exposures.

The oxidative potential of PM (F. Kelly)

The capacity of ambient PM to elicit oxidative stress in the lung, as well as systemically, has emerged as a unifying hypothesis to explain the health effects associated with air pollution (Gilliland et al., 1999; Kelly, 2003; Borm et al., 2007). Oxidative stress in the lung has been

shown to lead to acute symptoms such as impaired lung function and asthma exacerbations, as well as chronic injury characterized by impaired lung growth and accelerated declines in lung function. Asthmatics have decreased concentrations of antioxidants in their lung lining fluids that may explain their increased sensitivity to air pollutants. In this working paradigm inhaled particles generate oxidative stress through three inter-related pathways:

1. first, by direct introduction of oxidizing species into the lung, such as redox active transition metals or quinones absorbed on the particle surface;
2. by introducing surface absorbed PAHs that can undergo bio-transformation in vivo into quinones species through the action of the cytochrome P450, epoxide hydrolase and dihydrodiol dehydrogenase detoxification pathway; and
3. by stimulating inflammatory cells to undergo the oxidative burst.

Thus, variations in the surface metal and organic components of PM between locations with differing traffic contributions should result in altered PM oxidative potential. This hypothesis is being assessed in London following the introduction of the congestion charging scheme a traffic management scheme. Preliminary results indicate that particle composition does vary across the city and this is associated with changes in PM oxidative activity.

Recent studies on the impact of traffic-related air pollutants on atopic outcomes (J. Heinrich)

The last WHO review on health effects of transport-related air pollution (TAP) concluded that TAP increases the risk of respiratory symptoms and diseases that are not related to allergies, but such conclusion was not possible for allergic endpoints (WHO Regional Office for Europe, 2005). The heterogeneity in results of epidemiological studies on allergies might be partly caused by a lack of valid exposure strategies including individualized exposure assessments. A recent study used PM_{2.5} and sulfur content in PM_{2.5} per community in combination with the large database of the European Respiratory Health Survey. It did not show any association for allergic sensitized prevalence (Bedada et al. 2006) and confirmed previous findings on poor associations. Presumably the higher within-city variations of PM_{2.5} concentration than the between city contrasts lowered the chance to identify associations between TAP and allergic sensitization. Restriction of analysis to children attending a school close to a monitoring site did not show any increased risk for asthma (Hwang et al. 2005). However, birth cohort studies in the Netherlands and in Munich, Germany, which applied GIS-based individualized exposure models to estimate traffic-related pollution exposure showed consistently slightly increased risks of wheeze and asthma for PM_{2.5}, PM_{2.5} absorbance and nitrogen dioxide when the children reached an age of 4 and 2 years, respectively (Brauer et al. 2007, Morgenstern et al. 2007). Unpublished analyses of data of the same Munich cohort until the age of 6 years showed strong effects on asthma, hay fever, eczema and allergic sensitization against common aeroallergens. These effects were restricted to pollen, sensitization for PM_{2.5} and PM_{2.5} absorbance (Morgenstern et al. 2007). These recent findings indicate some evidence that traffic-related pollutants contribute to the development of asthma and allergies.

Studies on the relation of lung cancer to combustion related air pollution (P. Nafstad)

An increasing number of analytical epidemiological studies have found statistically significant associations between measures of exposure to ambient air pollution and lung cancer or death from lung cancer, suggesting that urban air pollution may be a risk factor for lung cancer. One example is the ACS study, where the investigators found a statistically significant association between area background levels of PM_{2.5} and death from lung cancer. Another example is a

recent case control study based on a cohort of 500 000 Europeans living in ten different countries. Area background levels of NO₂ were found to be associated with an increased risk of lung cancer. Lung cancer is a disease that develops over a long time period from the initiation through the development of cancer cells to symptoms, diagnosis and death. Hypothetically, several phases in this process could be affected by air pollution. However, the current epidemiological evidence is still too insufficient to be of much help when speculating at what point the disease process is affected, which biological mechanism is involved, and which pollutant could cause the effects. Optimal control for confounding is difficult due to the long disease process and insufficient knowledge about which parts of the process are of importance. Experience from air pollution epidemiology in Oslo, Norway (unpublished data) indicates that air pollution and measures of social deprivation on individual and neighborhood levels are correlated. Thus it is complicated to disentangle effects of air pollution from effects of social deprivation, at least with regard to mortality. The correlation might be a local phenomenon but the issue should be investigated further, perhaps also in other places in the world.

PM size as a health-related parameter

Fine and ultrafine particles and hospital admissions for cardiovascular and respiratory diseases in Rome (F. Forastiere)

There are few studies on health effects of fine and ultrafine particles in Europe. This presentation summarizes the impacts of outdoor PM₁₀, PM_{2.5} and ultrafine particles on hospital admissions for cardiovascular and respiratory diseases found by studies conducted in Rome.

The hospital admissions of residents of Rome in 2001–2005 were selected. Daily PM measurements were conducted at one monitoring station in the centre of Rome. Ultrafine particle number concentration (PNC), were measured with a TSI particle counter. PNC was correlated with PM₁₀ (0.57) and PM_{2.5} (0.55). A case-crossover design was adopted for the analysis using a time stratified approach to select control days; adjustment was made for apparent temperature, atmospheric pressure, holidays, and influenza epidemics. To assure comparability, the results are expressed as %age increase in admissions per 10 µg/m³ PM₁₀, 7 µg/m³ PM_{2.5}, and 6758 particles/cm³. The analysis was repeated by season: winter (December–March), summer (June–September), and spring/autumn (April, May, October and November).

The three PM indicators were associated with admissions for cardiac diseases at lag0, and the strongest effect was found for PM_{2.5} (0.98% increase, 95%CI: 0.49–1.48). However, PNC had a delayed effect on cardiac admissions (up to lag4, lag0–4, 0.85% increase, 95%CI: 0.32–1.39) that was not found for PM₁₀ and PM_{2.5}. The largest associations were found at lag 0 for PM_{2.5} and acute coronary syndrome (1.57% increase, 95%CI: 0.43–2.72) and heart failure (1.69%, 95%CI: 0.47–2.92). When respiratory diseases were evaluated, hospital admissions for asthma were associated with PM₁₀ (increase 3.25%, 95%CI: 0.59–5.97) at lag0, whereas PNC was associated with COPD admissions at lag0 (2.39%, 95%CI: 0.27–4.56) and bronchitis at lag2 (1.98%, 95%CI: 0.25–3.74).

In the seasonal analysis, PM_{2.5} was associated with admissions for cardiac diseases at lag0 in winter (1.77%, 95%CI: 0.85–2.69) and in spring/fall (1.62%, 95%CI: 0.18–3.08) but not in summer; on the other hand, the strongest effect of PM_{2.5} on respiratory diseases was in summer (lag0): 6.32% (95%CI: 0.22–12.79) for COPD and 21.74% (95%CI: 3.96–42.56) for asthma. The effect of PNC showed a delayed effect for cardiac diseases only in summer (2.43% at lag2) and an association with COPD admissions at lag0 was found in winter (1.73%, 95%CI: 0.02–3.47) and in spring/fall (2.99%, 95%CI: 0.52–5.52).

In summary, same day levels of $PM_{2.5}$ and ultrafine particles increases the risk of hospital admission for heart diseases; ultrafine particles have a delayed effect. Ultrafine particles are associated with hospital admissions for respiratory diseases, especially COPD. The effects of fine and ultrafine particles vary by season in a distinct way. $PM_{2.5}$ and PNC both had a cardiac effect during winter at immediate lag, but PNC also had a delayed effect during summer. $PM_{2.5}$ had the largest respiratory effect in summer whereas PNC was associated with COPD in winter and in the transition-period. The results may indicate that the effects are partially independent and have different mechanisms.

Parameters of ultrafine particles affecting their accumulation in secondary target organs (W.G. Kreyling)

To provide a rational base for the discussion of whether and to which extent PM may translocate across the air-blood-barrier of the respiratory tract into systemic circulation and subsequent accumulation in secondary target organs, the role of distinct parameters of various inhaled or instilled ultrafine particles with respect to subsequent particle translocation was studied. Sizes of instilled spherical gold nanoparticles (UFP) from 1.4 nm to 20 nm showed a strong inversely relation of translocation across the rat lung epithelium ranging from 6% of the deposited 1.4 nm UFP to 0.2% of the 20 nm UFP. In addition, surface charge of negatively versus positively charged 2.5 nm gold UFP led to significant change of the translocated fraction emphasizing the importance of UFP surface parameters as charge. Interestingly instilled 20 nm spherical gold UFP were translocated with the same fraction as inhaled same sized but chain agglomerated iridium UFP existing of 2–4 nm primary UFP and inhaled same sized chain agglomerated elemental carbon UFP existing of about 5 nm primary UFP. However, inhaled 20 nm chain agglomerated titanium dioxide particles were translocated at an order of magnitude larger fraction than all other 20 nm particles used emphasizing the importance of material differences. Micron sized particles are negligibly translocated across the air–blood barrier. Secondary target organs in which these UFP accumulate include liver, spleen, kidneys, heart, vasculature, brain, reproductive organs and even the fetus. The latter was shown for 1.4 and 20 nm gold UFP in pregnant rats at their third trimester of gestation. Limited human studies confirm that the translocated fraction of inhaled elemental carbon chain agglomerated UFP is not higher than in rats but lack identified fractions because of limits of detection.

Studies on health effects of coarse PM: the Saharan dust issue in Barcelona (N. Künzli)

Effective air quality abatement strategies in urban areas depend on local and regional mechanisms by which air pollution generates adverse health effects. The city of Barcelona in addition to present high concentrations of anthropogenic particulate matter, experiences winds which bring large amounts of dust from Sahara 7 to 15 times a year. Saharan dust episodes are a major recurrent air quality problem all across southern Europe. The objective of this study was to investigate whether outbreaks of Saharan dust exacerbate the health effects of anthropogenic PM, and how these effects relate to the chemical composition of particles. Effects on daily mortality of exposure to coarse particles ($PM_{10-2.5}$) compared to fine particles ($PM_{2.5}$) during the years 2003 and 2004 in Barcelona were investigated using a time-stratified case-crossover design. Effects modification during Saharan dust days were examined by including an interaction term in the multivariate models.

The study found that, considering all ages, the odds ratio for total mortality of the $PM_{10-2.5}$ fraction increased from 1.013 (95%CI: 0.992–1.034) during Non-Saharan dust days to 1.084 (95%CI: 1.015–1.158) during Saharan dust days with a p-value for interaction of 0.0515. No

statistical significant changes of effects were detected for $PM_{2.5}$. The change in toxicity does not seem to be explained by the change in concentrations of major and metal elements constituting the dust. This study suggests that health authorities should not assume that Saharan dust outbreaks are harmless events. Thus, to comply with the WHO guideline values set to protect public health, anthropogenic sources of particulate pollution need to be limited particularly rigorously in areas with Saharan dust episodes.

Toxicological studies on effects of size-segregated PM (R.O. Salonen)

The PAMCHAR project (<http://www.pamchar.org>) took a systematic approach in expanding the present knowledge on the source-specific chemical and toxicological characteristics of ambient air coarse ($PM_{10-2.5}$), fine ($PM_{2.5-0.2}$) and ultrafine ($PM_{0.2}$) particles. This included an optimization and validation of a high-volume cascade impactor (HVICI) as well as toxicological study protocols. Subsequently, contrasting particulate pollution situations in different geographical and seasonal conditions in Europe were examined with advanced high and low volume particulate sampling techniques and in-depth chemical analysis of the collected samples. The same size-segregated particulate samples, pooled from individual HVICI samples in each sampling campaign, were investigated and compared with each other in several well-established in vitro and in vivo test systems. $PM_{10-2.5}$ samples had a higher inflammatory activity than $PM_{2.5-0.2}$ and $PM_{0.2}$ samples in the mouse macrophage cell line RAW264.7, but $PM_{2.5-0.2}$ samples showed the largest differences in inflammatory activity, and $PM_{0.2}$ samples in cytotoxicity, between the sampling campaigns (Happo et al., 2007, Jalava et al., 2006, 2007). $PM_{0.2}$ sample from wintertime Prague with proven impacts from local coal and biomass combustion had very high cytotoxic and apoptotic activities and caused a distinct cell cycle arrest. In the lungs of healthy mice, exposed intratracheally and lavaged 4, 12 and 24 hours thereafter, $PM_{10-2.5}$ samples had a somewhat higher and longer-lasting inflammatory activity than $PM_{2.5-0.2}$ samples. $PM_{0.2}$ samples showed negligible inflammatory activity. Similarly to the in vitro studies in macrophage cell line, there was more heterogeneity in the inflammatory responses to $PM_{2.5-0.2}$ samples than to $PM_{10-2.5}$ samples between the sampling campaigns. In both the macrophage cell line and the mouse lung, $PM_{2.5-0.2}$ samples from springtime Barcelona and summertime Athens had the highest inflammatory activities, which may be related to the highest atmospheric photochemical activity and transformation of organic compounds observed during these sampling campaigns. In addition, the transition metal (Cu, Ni, V, Fe) content of $PM_{2.5-0.2}$ samples, and the endotoxin content of $PM_{10-2.5}$ samples, may contribute to the inflammatory activities. The lowest in vitro and in vivo inflammatory activity and highest cytotoxic activity of $PM_{2.5-0.2}$ samples from wintertime Prague may be related to the measured high content (>50%) of carbonaceous material like elemental carbon and organic matter (including polycyclic aromatic hydrocarbons (PAH)) originating from poor local combustion. The inflammatory and cytotoxic activities of both the $PM_{10-2.5}$ and $PM_{2.5-0.2}$ samples from all the six sampling campaigns were to large extent associated with the water-insoluble particulate fraction. Thus, particulate size, sources and atmospheric transformation processes affect the chemical composition and toxicity of urban aerosols in a complex manner.

Chemical characteristics of PM as a health-related parameter

The effects of fine particle speciation daily mortality and morbidity in California (B. Ostro)

Several epidemiological studies provide evidence of an association between daily mortality and $PM_{2.5}$. Little is known, however, about the relative effects of $PM_{2.5}$ constituents. The associations between daily mortality and 13 components $PM_{2.5}$, including elemental and organic carbon (EC and OC), nitrates, sulfates, and various metals in six California counties from 2000 to 2003 were

examined. Poisson regressions incorporating natural splines were used to control for time-varying covariates. Effect estimates were determined for each component in each county and then combined using a random effects meta-analytic model. PM_{2.5} mass and several constituents (EC, nitrates, sulfates, iron, zinc and potassium) were associated with multiple mortality categories, especially cardiovascular deaths. Using the interquartile range, a single-day lag in these pollutants was associated with about a 2% change in daily mortality. This multicounty analysis adds to the growing body of evidence linking PM_{2.5} with mortality and indicates that excess risks may vary among specific PM_{2.5} components. The findings support the hypothesis that combustion-associated pollutants from diesel and gasoline engines and from wood smoke are associated with severe health outcomes in California.

Effects of transition metals and metallic compounds (M. Lippmann)

While the average annual concentrations of PM_{2.5} mass in United States metropolitan areas vary by less than a factor of 2, there are much larger variations in the concentrations of components as illustrated in the spatial maps that were prepared using speciation network data for source apportionment that were presented at the Workshop. They showed pronounced peaks for soil PM in Phoenix, motor vehicle PM in Los Angeles, coal combustion PM in Pittsburgh, and residual oil combustion PM in New York and other port cities on the Atlantic, Pacific and the Great Lakes.

The residual oil combustion effluent, which is characterized by its content of Ni and V has been significantly associated with: excess monthly mortality and bronchial hyper-reactivity in Hong Kong Special Administrative Region China, excess daily mortality in 60 US cities (Lippmann et al., 2006), and with NF κ B activity in human lung cells in vitro in Sterling Forest, a large state park north-west of New York City (Maciejczyk & Chen, 2005). The in vitro study was done in parallel with a subchronic inhalation study in which a mouse model of atherosclerosis (ApoE^{-/-}) and normal mice were exposed to either PM-free air or PM_{2.5} that was concentrated 10 times for 6 hours/day, 5 days/week, for 6 months. In the ApoE^{-/-} mice there were PM_{2.5} exposure-related effects in both acute and progressive changes in heart rate (HR) and HR variability (HRV) and, at the end of the exposures, increases in aortic plaque size and invasiveness, alterations in brain cell distribution and genetic markers (Lippmann et al., 2005). In a second 6 month concentrated ambient particles (CAPs) inhalation study in Sterling Forest, similar responses were received, various biomarkers for inflammation were identified (Sun et al. 2005). It was also noted that there were 14 days with unusually high deviations in HR and HRV, that the concentrations of Ni, Cr and Fe were greatly elevated while PM_{2.5} and all other measured elements (including V) were unusually low. Back-trajectory analyses identified the large Ni smelter in Western Ontario with a very tall stack as the likely source for the three metals (Lippmann et al. 2006)

Unpublished results from further analyses of subchronic CAPs inhalation studies at Sterling Forest were also presented. CAPs collected for the Maciejczyk & Chen (2005) study were composited into 2 samples; one for 12 days with a high NF κ B response in lung cells, and the other for 36 days with very low NF κ B responses. The high-response composite, which was greatly elevated in Ni and V, produced in vitro elevations in a variety of biomarkers in microglial cells that were not seen in the low NF κ B response composite. In another CAPs study involving 10 weeks of exposure in normal mice (C57Bl) on a high-fat diet, the CAPs exposures produced steatohepatitis in the liver.

Secondary inorganic aerosols and health effects – Evidence from toxicology (M. Gerlofs-Nijland)

Although PM has been associated with adverse health effects it is not yet clear which constituents are responsible for these adverse effects. A major part of the ambient PM consists of the so called secondary inorganic aerosol (SIA), which originates from sulfur dioxide and nitrogen and water. This results in acid aerosols, which are often neutralized by ammonia to form ammonium salts. Power plants and motor vehicle exhaust including road traffic and shipping are the main sources of respectively sulfates and nitrates. Reducing this part of the PM would have a significant impact on meeting the PM standards. However, the key question is: is there a toxicological basis for a causal relationship between sulfates or nitrates and human health effects associated with exposure to ambient PM. The health impacts of SIAs were reviewed (Schlesinger & Cassee, 2003; Reiss et al., 2007). There are only a few epidemiological studies that have included sulfates in their analysis. There are even less studies for nitrate. In general the associations with mortality are weaker for sulfate compared to PM_{2.5} (Reiss et al., 2007). Furthermore, the calculated relative risks for sulfate are influenced by gases indicated by smaller risk estimates in multi pollutant models. Overall, the outcomes of epidemiological studies with sulfate are inconsistent and not as robust as for PM₁₀ (Reiss et al., 2007). Concerning toxicology, responses in the respiratory tract were noted to occur in relation to the acidity of the exposure atmosphere and not to the mass, and no systemic effects are known after inhalation. As part of the whole complex PM mixture, the outcomes were inconsistent with regards to the effects of sulfate and nitrate (Reiss et al., 2007). Significant associations with sulfate could point towards possible indirect effects like e.g. increased bioavailability of toxic components influenced by acidity. In conclusion, there is no large burden of evidence to prove that sulfate is the real causal agent. Like PM, sulfate should be considered as an indicator rather than a causal constituent. Very little is known about nitrates though, like sulfate, it is an endogenous chemical which suggest that any effect can probably be contributed to a co-factor such as organics or metal ions. SIA is a part within ambient PM which is of lesser health concern compared to other parts. However, by reducing SIA levels and without a reduction of current standards, the health problems will not be solved and it will open opportunities for increases in more toxic components before the standard is reached. Therefore, reducing secondary inorganic aerosol could be favoured as a policy to reduce acidification but could have a negative effect on health.

Study designs to identify health-relevant PM sources

The HEI National Particle Component Toxicity Initiative – HEI NPACT (A. Cohen)

In January 2007, HEI began HEI NPACT to answer a key question regarding the effects of PM on health: Are all components of PM from all sources equally toxic, or are some of more concern and deserving of greater attention? Answering this question will require comprehensive and balanced scientific collaboration, designed to provide results for use in future decisions about United States national ambient air quality standards and state implementation plans. This multidisciplinary effort combines data from HEI's national Web-based air-quality database (<http://hei.aer.com>); high-quality scientific research projects selected from applications by many expert groups in the United States and Europe; broad support in the US Environmental Protection Agency and a range of key industry sectors; and timely reporting to inform the next rounds of decisions on the regulation of PM.

HEI NPACT will be conducted by three teams selected via a competitive process. Teams at the University of Washington/Lovelace Respiratory Research Institute and New York University will conduct integrated toxicologic and epidemiologic studies in cities across the United States with differing compositions of PM and levels of gaseous pollutants. Together these teams will

perform toxicologic studies in 12 locations across the country and epidemiologic studies in more than 100 cities in order to examine how PM components and gases may be related to health. A third group at Yale University will estimate the short-term effects of PM components and gases on mortality in more than 200 US cities, using data from the National Morbidity, Mortality, and Air Pollution Study (NMMAPS).

HEI NPACT will incorporate intensive study management and peer review meeting HEI's rigorous standards for oversight and quality assurance. Reports of results will be provided not only in scientific detail but also in concise, comprehensible summaries for decision-makers at the federal and state levels and for other stakeholders. Initial results are expected in late 2009 and 2010. Comprehensive results of all studies are expected in 2011 and 2012.

Source characterization in the MESA Air study and WHI (S. Dubowsky-Adar)

The University of Washington (Seattle, United States) has begun an investigation regarding compositional features of ambient fine PM (PM_{2.5}) and cardiovascular disease. This research is being conducted within two major prospective cohort studies that collect detailed information on cardiovascular health, the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air) and the Women's Health Initiative Observational Study (WHI-OS). The primary objective of this project is to identify the chemical components and sources of ambient PM_{2.5} that contribute to the effects of long-term exposure on incident cardiovascular events and the extent and progression of atherosclerosis as measured by carotid intima-media thickness and coronary artery calcification. Although atherosclerosis is only measured within the MESA Air cohort, cardiovascular risk factors and clinical events are extremely well characterized in both cohorts (> 7000 participants in MESA Air and 90 000 women in WHI-OS), especially as compared to past projects in the air pollution field. Estimates of exposure at each participant's residence will also be estimated using land use regression and spatio-temporal modelling approaches based on data from nationwide fine PM_{2.5} speciation networks and intensive supplemental monitoring undertaken specifically for MESA Air and this project. Such data collection is ongoing and early analyses have demonstrated substantial variations in exposure to certain components both between- and within-metropolitan areas. The potential significance of this project is substantial as the identification of the most important components of PM and the corresponding sources of these components will enable more focused and thereby more efficient efforts at prevention.

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