NPACT: Particulate Matter Components Associated with Health Effects

BACKGROUND

Extensive epidemiologic evidence, as well as toxicologic evidence, supports an association between air pollution exposure and adverse health effects, in particular cardiovascular disease (CVD). In order to gain an insight as to whether certain components of the particulate matter (PM) mixture may be responsible for its toxicity and human health effects, HEI funded the National Particle Component Toxicity (NPACT) Initiative. The Initiative consisted of coordinated epidemiologic and toxicologic studies to evaluate the relative toxicity of various chemical and physical properties of PM and selected gaseous copollutants. The lead investigators were Drs. Morton Lippmann (this report) and Sverre Vedal (HEI Research Report 178). Given the well documented associations between ambient PM concentrations and cardiovascular mortality and morbidity, the NPACT studies focused primarily on health outcomes and biologic markers related to CVD.

APPROACH

Lippmann and colleagues at New York University conducted four toxicologic and epidemiologic studies to determine short- and long-term health effects associated with PM and its components. Study 1, led by Lung-Chi Chen, analyzed heart rate variability (HRV) and atherosclerosis in mice exposed for 6 months by inhalation to fine concentrated ambient particles (CAPs) in five geographic regions in the United States. Study 2, led by Terry Gordon, measured acute changes in markers of inflammation and oxidative stress in mice and in human cell lines exposed to a large number of PM samples collected at the same five locations as in the Chen study, focusing on metal composition and PM size classes (coarse, fine, and ultrafine). Study 3, led by Kazuhiko Ito, used data from the U.S. Environmental Protection Agency’s Chemical Speciation Network (CSN) in a time-series analysis of all-cause mortality and hospital admissions associated with specific source categories of PM ≤ 2.5 µm in aerodynamic diameter (PM$_{2.5}$) in 150 U.S. cities. Study 4, led by George Thurston, also used CSN data to evaluate associations between long-term exposure to PM components and mortality from CVD.

What This Study Adds

- In this comprehensive and ambitious study, Lippmann and colleagues performed coordinated epidemiologic and toxicologic studies of the health effects of PM and its components. They conducted studies in mice and in human cell lines exposed to ambient PM and epidemiologic studies of short- and long-term cardiovascular effects. These studies mark an important addition to research on air quality and health.
- This study has provided new insights into the toxicity of components and source categories, and identified the Coal Combustion, Residual Oil Combustion, Traffic, and Metals source categories as most consistently associated with health effects. However, other components and source categories could not be definitively excluded as having no adverse effects.
- Better understanding of exposure and health effects is needed before it can be concluded that regulations targeting specific sources or components of PM$_{2.5}$ will protect public health more effectively than continuing to follow the current practices of targeting PM$_{2.5}$ mass as a whole.
Results presented are those that demonstrated the most consistently positive associations; the remaining results were not positive or significant. Gray and black diamonds depict results from the random effects Cox models without and with contextual ecologic covariates, respectively. Note that the IQR (interquartile range) varied by pollutant; e.g., the IQRs for PM_{2.5} and sulfur were 3.13 µg/m^3 and 0.53 µg/m^3, respectively.
The Panel noted that the results of Study 3 support associations of daily mortality and hospital admissions with both traffic-related pollutants and secondary aerosols. The Panel emphasized that some results should be interpreted with caution because a high proportion of the data for important PM components (e.g., nickel, arsenic, copper, and vanadium) was below the limit of detection or had low monitor-to-monitor correlations. The patterns of correlations between pollutants were complicated, and it was difficult to interpret their potential effects on associations with health effects.

**Study 4** In this cohort study, Thurston and colleagues found the strongest associations for mortality with the Coal Combustion and Traffic source categories and with sulfur, which strongly contributed to both of those categories, and EC, the primary contributor to Traffic. The associations of Traffic and EC with mortality were, however, highly sensitive to the inclusion of ecologic covariates in the analyses and to the use of a random effects Cox model instead of a standard Cox proportional hazards model (see the figure). The investigators concluded that long-term exposure to PM$_{2.5}$ and the Coal Combustion source category explained most of the associations of exposure to PM$_{2.5}$ with all-cause, ischemic heart disease, and lung cancer mortality (but not respiratory mortality).

The Panel noted that Study 4 yielded many important results during the extended follow-up period of the CPS-II cohort. However, the Panel was not convinced that the study has definitively demonstrated that long-term exposure to components of PM$_{2.5}$ is more important than exposure to total PM$_{2.5}$ in causing adverse effects. Although the Panel agreed that the investigators found the most consistent associations with the Coal Combustion source category, the Panel disagreed with the investigators’ conclusion that exposure to coal combustion emissions is more strongly associated with mortality than exposure to traffic emissions, because traffic is one of the most important contributors to within-city differences in PM$_{2.5}$ exposure; however, this is not well captured by the limited number of monitors within a city. The Panel also noted other issues, such as a decreasing trend in coal combustion emissions over the past decades.

Although the Total Risk Index analysis provided some interesting results that suggested that exposure to combinations of components and gases in pollutant mixtures is potentially more toxic than exposure to PM$_{2.5}$ mass alone, the Panel thought that the approach, although promising, had some problems that precluded considering these results to be more than suggestive.

**CONCLUSIONS**

Lippmann and colleagues conducted a comprehensive research program to evaluate the relative toxicity of PM$_{2.5}$ components and source categories. The findings identified Coal Combustion, Residual Oil Combustion, Traffic, and Metals source categories as most consistently associated with health effects. However, the Panel thought that the study has not shown conclusively that specific components or sources were more definitively associated with health outcomes than other components or sources.

**SYNTHESIS OF NPACT STUDIES BY LIPPMANN AND VEDAL**

This section looks broadly at the approaches and results of the reports by Drs. Lippmann and Vedal and considers whether there is coherence and consistency in the epidemiologic and toxicologic results.

Both studies found that adverse health outcomes were consistently associated with sulfur and sulfate (markers primarily of coal and oil combustion) and with
traffic-related pollutants, although the relative importance of the latter remains unclear because exposure to traffic-related pollutants varies within metropolitan areas and thus is more subject to uncertainty than exposure to pollutants from other source categories. The results for sulfur and sulfate may have been more consistent because their concentrations were more accurately estimated (due to their spatial homogeneity) than concentrations of other pollutants.

Biomass combustion, crustal sources, and related components were not generally associated with short- or long-term epidemiologic findings in these studies, but there were only a limited number of cities where these sources and components were likely to be measured consistently. The possibility remains that biomass combustion contributed to OC concentrations, and thus to its associations with cardiovascular outcomes. There were few consistent associations with other components or sources, although the Panel cautions that this is not conclusive evidence that these components and sources do not have adverse health effects. Further analyses of some of these sources are warranted.

Both studies highlight how important the CSN is to research on the health effects of components of air pollution and to air quality management. Neither study could have been performed without CSN data, although the studies highlighted some limitations that suggest that further efforts would be helpful to characterize EC, OC, and metals (i.e., combustion- and traffic-related components); to lower the detection limits of some components; and to collect daily measurements.

The NPACT studies, which are to date the most systematic effort to combine epidemiologic and toxicologic analyses of these questions, found associations of secondary sulfate and, to a somewhat lesser extent, traffic sources with health effects. But the Panel concluded that the studies do not provide compelling evidence that any specific source, component, or size class of PM does not play a role in toxicity. If greater success is to be achieved in isolating the effects of pollutants from mobile and other major sources, either as individual components or as a mixture, more advanced approaches and additional measurements will be needed so that exposure at the individual or population level can be assessed more accurately. Such enhanced understanding of exposure and health effects will be needed before it can be concluded that regulations targeting specific sources or components of PM$_{2.5}$ will protect public health more effectively than continuing to follow the current practice of targeting PM$_{2.5}$ mass as a whole.