HEI

STATEMENT

Synopsis of Research Report 138

HEALTH EFFECTS INSTITUTE

Health Effects of Real-World Exposure to Diesel Exhaust in Persons with Asthma

BACKGROUND

In the 1990s, results from several epidemiologic and controlled-exposure studies suggested an association between exposure to air pollution from traffic-derived particulate matter (PM) and increases in symptoms of airway diseases, including exacerbations of asthma. Some results also suggested that exhaust from diesel engines, used in a large fraction of vehicles worldwide and particularly in Europe, contributed to these effects. In response to HEI RFA 00-1, *Effects of Diesel Exhaust and Other Particles on the Exacerbation of Asthma and Other Allergic Diseases,* Dr. Junfeng (Jim) Zhang of the University of Medicine and Dentistry of New Jersey, proposed a study that would investigate how inhaling air with a high concentration of diesel exhaust from vehicular traffic while walking on a street in Central London, United Kingdom, might affect people who had either mild or moderate asthma. Dr. Zhang and his colleagues hypothesized that this exposure would exacerbate asthma symptoms, decrease lung function, and induce lung inflammation and oxidative stress responses. The HEI Research Committee recommended Dr. Zhang's proposal for funding.

APPROACH

The investigators recruited 60 nonsmoking participants of both sexes between 18 and 55 years old, with mild or moderate asthma. Each subject participated in one 2-hour exposure session by walking along Oxford Street, a busy Central London thoroughfare where vehicles are predominantly diesel-powered, and one 2-hour session walking at a nearby control site, Hyde Park, where there is no traffic.

Before, during, and after each session, the investigators evaluated pulmonary function parameters (forced expiratory volume in the first second [FEV_1], forced vital capacity [FVC], and forced expiratory flow during the middle half of the FVC [$FEF_{25–75}$]) and asthma symptoms. At some time points Zhang and colleagues also evaluated bronchial reactivity (PC_{20}) and markers of airway inflammation and oxidative stress. These markers included exhaled nitric oxide, the pH of exhaled breath condensate (EBC), blood thiobarbituric acid reactive substances (TBARS), sputum interleukin-8 and myeloperoxidase (MPO). Participants kept a record of asthma symptom scores, peak expiratory flow rate (PEFR), and asthma reliever medication use during the 7 days before and after each session.

Pollutant samplers, placed on a cart that accompanied the participants during sessions, measured concentrations of $PM_{2.5}$ ($PM \leq 2.5$ µm in aerodynamic diameter), ultrafine particles (UFP; PM < 100 nm in aerodynamic diameter), elemental carbon (EC), and nitrogen dioxide (NO_2).

STATISTICAL METHODS

Zhang and colleagues used two main statistical approaches: comparative analyses between the exposure and control sessions that took advantage of the paired design of the study to compare within-subject responses, and pollutant-specific exposure–response analyses that estimated associations between the concentration of an individual pollutant and a change in a health endpoint from its baseline value. In one set of pollutant-specific exposure–response analyses, each of the four pollutants was used as a single covariate; a second

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Junfeng Zhang, University of Medicine and Dentistry of New Jersey–School of Public Health. The complete report, *Health Effects of Real-World Exposure to Diesel Exhaust in Persons with Asthma*, can be obtained from HEI or our Web site (see contact information last page).

set of analyses used two of the four pollutants as covariates. They analyzed responses for all subjects, and also analyzed responses separately for participants with either mild or moderate asthma.

RESULTS

The investigators found that participants were exposed to higher average pollutant concentrations during the exposure session than during the control session: approximately 5-fold higher EC, 4-fold higher NO_2, 3.5-fold higher UFP, and 2-fold higher $PM_{2.5}$ mass.

FEV_1 and FVC were significantly lower after the exposure session compared with the control session (stratified analyses showed that these effects were dominated by responses in participants with moderate asthma). However, $FEF_{25–75}$ and PEFR did not differ significantly. Also not affected by exposure were asthma symptom scores, asthma medication use, PC_{20}, and blood TBARS; some of these responses showed nonsignificant trends. A significant relative decrease in EBC pH of 2.0% (correlating with an approximate half-log change in pH) was noted one hour after the exposure session; this effect was also dominated by observations in subjects with moderate asthma. Of the sputum parameters evaluated, only the neutrophil-associated enzyme MPO differed significantly with a 5-fold increase after the exposure session compared with after the control session.

In one-pollutant exposure–response analyses, UFP and NO_2 were associated with changes in the most endpoints, EC with fewer, and $PM_{2.5}$ with fewer still. In two-pollutant models, several associations between the measured pollutants and changes in endpoints lost significance after the investigators controlled for other pollutants. Some associations, however, were unaffected by the inclusion of a second pollutant. Associations of UFP with endpoints were not affected by adjusting for other pollutants, except NO_2. Adjusting for NO_2 generally appeared to reduce associations with the other pollutants.

SUMMARY AND CONCLUSIONS

The study by Zhang and colleagues, with an innovative approach, has provided interesting new findings. The effects with the most potential clinical significance were the relative decreases in FEV_1 (3.0%–4.1%) and FVC (3.1%–3.7%) during and several hours after the exposure ended. The magnitude of these decrements in lung function may be clinically relevant for patients with severe or uncontrolled asthma, whose lung capacity is severely diminished compared with healthy people.

Based on the statistically significant changes in one marker each of airway inflammation (MPO) and of airway acidification (EBC pH), and in conjunction with sputum findings of marginal statistical significance, results of this study suggest that the exposure session was associated with a mild increase in inflammatory response in the airways that was mediated by neutrophils.

Asthma symptoms and the use of asthma reliever medication increased only marginally after the exposure session. Thus, whereas exposure to a diesel-traffic–enriched environment may have produced changes in pulmonary function and inflammatory endpoints, the lack of significant changes in symptoms or the use of asthma reliever medication suggests that this single exposure did not affect the clinical status of asthmatic participants.

Analyses with stratification by the severity of asthma showed that changes in FEV_1, FVC, and EBC pH were significant only in subjects with moderate asthma. Because the majority of subjects with moderate asthma were taking corticosteroids, it is possible that corticosteroid use may have blunted responses in this group. Though the background severity of asthma may be an important factor affecting responses to diesel traffic exposure, further work is needed to confirm or disprove this hypothesis.

Exploratory one- and two-pollutant analyses to identify associations between specific components of the pollutant mix and changes in endpoints found that UFP and NO_2 were associated with the most endpoints, EC with fewer, and $PM_{2.5}$ with fewer still. All these pollutants are constituents of traffic emissions and EC is frequently used as a marker of diesel emissions, but none is absolutely specific to diesel. Thus, because the pollutants measured are not specific to diesel emissions, the results are only suggestive of the effects of DE on the endpoints measured.

Explanations for the effects observed, other than exposure to DE, also need to be borne in mind. One is that participants were almost certainly concurrently exposed to air pollutants not associated with diesel-powered engines, such as pollutants derived

from tailpipe emissions of gasoline-powered cars on streets that cross Oxford Street, as well as particles not derived from tailpipe emissions — such as those generated by tire and brake wear and roadway dust produced by all vehicles. In addition, concentrations of several traffic-associated pollutants (including CO, organic carbon compounds, and particles in the coarse size range) were not measured in the current study and may be associated with the endpoints evaluated. Furthermore, the exposure and control sites differed in other, unmeasured characteristics, particularly in noise levels and the amount of stress experienced by the subjects.

Although the findings of the current study indicate that lung function is slightly decreased and some markers of airway inflammation are increased in people with asthma who are exposed to ambient urban air in a roadside environment dominated by diesel vehicles, the study does not provide direct evidence that DE itself causes these effects. Additional studies would be needed to address that question, and to identify specific components of DE that might be responsible for any observed health effects. A final consideration is that since the study was completed, more stringent emissions and fuel standards have been implemented and new engine technologies introduced in both the United States and Europe. As older vehicles are replaced in the fleet, decreases in most traffic-related pollutant concentrations can be anticipated. The health impact of these changes will need to be assessed; this study may serve as a baseline analysis for future studies on the effects of such changes.

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Junfeng (Jim) Zhang, James E. McCreanor, Paul Cullinan, Kian Fan Chung, Pamela Ohman-Strickland, In-Kyu Han, Lars Järup, and Mark J. Nieuwenhuijse

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INVESTIGATORS' REPORT *by Zhang et al.*

Continued

COMMENTARY *by the Health Review Committee*

HEALTH EFFECTS INSTITUTE

101 Federal Street, Suite 500
Boston, MA 02110, USA
+1-617-488-2300 phone
+1-617-488-2335 fax

pubs@healtheffects.org
www.healtheffects.org

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