Commentary: Nitrogen dioxide and asthma redux

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Nitrogen dioxide (NO\textsubscript{2}), a combustion-generated oxidant gas, is widely present in indoor and outdoor environments. Outdoors, where it comes primarily from combustion engines, industry, and power generation, it is a precursor to particles and ozone. Indoors, NO\textsubscript{2} is generated by gas cooking and heating, and it exists as a gas along with other oxides of nitrogen. Many epidemiological studies have examined effects of NO\textsubscript{2} outdoors and indoors on risk for lower respiratory infection, asthma, and other respiratory diseases and conditions. Evidence from studies of outdoor air pollution cannot readily isolate an effect of NO\textsubscript{2} because of its contribution to the formation of secondary particles and ozone. Observational studies of exposure indoors can test hypotheses related to NO\textsubscript{2} specifically, although confounding by combustion sources in the home is a concern. In this issue of the International Journal of Epidemiology, Pilotto and colleagues\textsuperscript{1} present the findings of a trial to reduce exposures to indoors, NO\textsubscript{2}, a design that potentially avoids confounding and selection bias.

The study addressed asthma, a highly prevalent disease in Australia, and exposure to NO\textsubscript{2} in classrooms that are heated by unvented space heaters, a common mode of space heating in some parts of Australia.\textsuperscript{2} The unvented heaters were replaced at random in 8 of 18 participating schools. Spengler \textit{et al}.\textsuperscript{2} have previously shown that NO\textsubscript{2} exposures may be substantial for children in New South Wales, Australia, who are exposed to unvented combustion heaters at home and at school. The new study provides persuasive evidence of an association between exposure to NO\textsubscript{2} from in-class heaters and the respiratory health of children with asthma.

Although studied extensively, the toxicological and epidemiological evidence on NO\textsubscript{2} and asthma has been mixed. As an oxidant gas that reaches the small airways of the lung, adverse effects of exposure would be anticipated, but controlled exposures of volunteers with asthma have not consistently shown adverse effects.\textsuperscript{3,4} Previous population studies of NO\textsubscript{2} exposure have been largely observational in design. In the 1960s and 1970s, epidemiological studies of the health effects of NO\textsubscript{2} focused primarily on ambient exposure. Subsequently, most of the evidence on NO\textsubscript{2} came from studies of indoor exposures, primarily from gas stoves.\textsuperscript{5} In a 1999 review, Samet and Basu\textsuperscript{4} found the evidence to be mixed across the array of outcome measures considered in these studies, including asthma.

Epidemiological studies in Australia have generally shown adverse effects of NO\textsubscript{2} exposure, perhaps reflecting higher levels of exposure. A 1997 observational study of NO\textsubscript{2} exposure in classrooms in Australia found that children attending schools with unflued gas heating had significantly higher frequencies of sore throat, colds, and school absenteeism, as well as higher NO\textsubscript{2} exposure, than children attending schools with electric heating.\textsuperscript{5,6} In a study of South Australian preschool children, there was weak evidence that NO\textsubscript{2} was associated with asthma prevalence.\textsuperscript{7,8} In a study in Victoria, Australia, NO\textsubscript{2} levels in the home were associated with respiratory symptoms, even though the levels were relatively low.\textsuperscript{9} In a panel study of children with asthma, personal exposure to NO\textsubscript{2} was positively associated with symptoms.\textsuperscript{10}

Two recent studies from outside Australia are also relevant. Chauhan and colleagues\textsuperscript{11} followed a cohort of asthmatic children in the UK, measuring personal NO\textsubscript{2} exposures weekly for up to 13 months. For illness episodes, viral cultures were obtained and the severity of the illness assessed. Comparing high with low NO\textsubscript{2} exposures in the prior week, NO\textsubscript{2} was associated with more severe illness. In a birth cohort of US infants having an asthmatic sibling, exposure to a gas stove and measured NO\textsubscript{2} levels were associated with increased risk for wheeze and cough in the first year of life.\textsuperscript{12}

The new study by Pilotto \textit{et al}.\textsuperscript{1} complements these previous studies, adding evidence from an intervention and thus avoiding some potential limitations of observational studies on this same exposure. While children and their parents may have been aware that a school’s heating system had been replaced, they were not aware that the change was related to the study. Thus, the benefit of heater replacement is unlikely to be due to information bias. The two groups of children had similar baseline characteristics, including parental smoking, gender, and asthma medication use; thus, confounding also is unlikely to explain the findings. The concentrations of NO\textsubscript{2} in the home environment, measured in kitchens and through personal monitoring, were similar for the two groups, implying that exposure at school was likely to be the primary determinant of a difference in indoor NO\textsubscript{2} exposure between the two groups. Together, this study and the other recent reports provide consistent evidence for an adverse effect on asthma.

The study of Pilotto \textit{et al}.\textsuperscript{1} demonstrates that replacement of unflued gas heaters can be effective in reducing NO\textsubscript{2} exposure for Australian schoolchildren. Concentrations of NO\textsubscript{2} in the Australian schools with unflued heaters ranged from 12 to 116 ppb, with a mean of 47.0 ppb; when compared with other locations in a multi-city study, these figures were higher than indoor levels measured in 17 cities in 15 countries, except for Mexico City.\textsuperscript{13} Replacement of the unflued heaters in the

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Australian schools lowered NO₂ concentrations by an average of 31.5 ppb. The study by Pilotto and colleagues\(^1\) provides a rationale for moving forward with replacing unflued heaters in classrooms.

References

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